Connecting via Winsock to STN

Welcome to STN International! Enter x:X

LOGINID:ssptacrs1614

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS	1		Web Page for STN Seminar Schedule - N. America
NEWS	2	AUG 06	CAS REGISTRY enhanced with new experimental property tags
NEWS	3	AUG 06	FSTA enhanced with new thesaurus edition
NEWS	4	AUG 13	CA/CAplus enhanced with additional kind codes for granted patents
NEWS	5	AUG 20	CA/CAplus enhanced with CAS indexing in pre-1907 records
NEWS	6	AUG 27	Full-text patent databases enhanced with predefined patent family display formats from INPADOCDB
NEWS	7	AUG 27	USPATOLD now available on STN
NEWS	8	AUG 28	CAS REGISTRY enhanced with additional experimental spectral property data
NEWS	9	SEP 07	STN AnaVist, Version 2.0, now available with Derwent World Patents Index
NEWS	10	SEP 13	FORIS renamed to SOFIS
NEWS	11	SEP 13	INPADOCDB enhanced with monthly SDI frequency
NEWS	12	SEP 17	CA/CAplus enhanced with printed CA page images from 1967-1998
NEWS	13	SEP 17	CAplus coverage extended to include traditional medicine patents
NEWS	14	SEP 24	EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS	15	OCT 02	CA/CAplus enhanced with pre-1907 records from Chemisches Zentralblatt
NEWS	16	OCT 19	BEILSTEIN updated with new compounds
NEWS	17	NOV 15	Derwent Indian patent publication number format enhanced
NEWS	18	NOV 19	WPIX enhanced with XML display format
NEWS	19	NOV 30	ICSD reloaded with enhancements
NEWS	20	DEC 04	LINPADOCDB now available on STN
NEWS	21	DEC 14	BEILSTEIN pricing structure to change
NEWS	22	DEC 17	USPATOLD added to additional database clusters
NEWS	23	DEC 17	IMSDRUGCONF removed from database clusters and STN
NEWS	24	DEC 17	DGENE now includes more than 10 million sequences
NEWS	25	DEC 17	TOXCENTER enhanced with 2008 MeSH vocabulary in MEDLINE segment
NEWS	26	DEC 17	MEDLINE and LMEDLINE updated with 2008 MeSH vocabulary
NEWS	27	DEC 17	CA/CAplus enhanced with new custom IPC display formats
NEWS	28	DEC 17	STN Viewer enhanced with full-text patent content from USPATOLD
NEWS	29	JAN 02	STN pricing information for 2008 now available
NEWS	30	JAN 16	CAS patent coverage enhanced to include exemplified prophetic substances

NEWS EXPRESS 19 SEPTEMBER 2007: CURRENT WINDOWS VERSION IS V8.2, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 19 SEPTEMBER 2007.

NEWS HOURS STN Operating Hours Plus Help Desk Availability

```
 NEWS LOGIN    Welcome Banner and News Items
 NEWS IPC8     For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that
specific topic.

  All use of STN is subject to the provisions of the STN Customer
  agreement.  Please note that this agreement limits use to scientific
  research.  Use for software development or design or implementation
  of commercial gateways or other similar uses is prohibited and may
  result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 08:37:11 ON 22 JAN 2008

=> file registry
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                             ENTRY    SESSION
FULL ESTIMATED COST                                           0.21       0.21

FILE 'REGISTRY' ENTERED AT 08:37:32 ON 22 JAN 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2008 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   21 JAN 2008  HIGHEST RN 1000370-19-3
DICTIONARY FILE UPDATES:  21 JAN 2008  HIGHEST RN 1000370-19-3

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=> e methy-th
E1          170     METHUSELAH/BI
E2         1596     METHY/BI
E3            0 --> METHY-TH/BI
E4            1     METHYB/BI
E5            1     METHYBOL/BI
E6            1     METHYBROM/BI
E7            3     METHYCAINE/BI
E8            1     METHYCILLIN/BI
E9            1     METHYCLO/BI
E10           1     METHYCLOTHI/BI
E11           1     METHYCLOTHIAZI/BI
E12           1     METHYCLOTHIAZID/BI

=> file caplus
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
```

	ENTRY	SESSION
FULL ESTIMATED COST	0.46	0.67

FILE 'CAPLUS' ENTERED AT 08:37:59 ON 22 JAN 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 22 Jan 2008 VOL 148 ISS 4
FILE LAST UPDATED: 21 Jan 2008 (20080121/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html

```
=> s (ido or 1mt or indoleamine) and inhibitor
          1168 IDO
            22 IDOS
          1187 IDO
                 (IDO OR IDOS)
            32 1MT
          1981 INDOLEAMINE
           742 INDOLEAMINES
          2344 INDOLEAMINE
                 (INDOLEAMINE OR INDOLEAMINES)
        562807 INHIBITOR
        565010 INHIBITORS
        882264 INHIBITOR
                 (INHIBITOR OR INHIBITORS)
L1         431 (IDO OR 1MT OR INDOLEAMINE) AND INHIBITOR

=> s l1 and (cancer or tumor or neoplasm)
        344399 CANCER
         50644 CANCERS
        357231 CANCER
                 (CANCER OR CANCERS)
        437225 TUMOR
        164827 TUMORS
        488179 TUMOR
                 (TUMOR OR TUMORS)
        479640 NEOPLASM
         36935 NEOPLASMS
        496541 NEOPLASM
                 (NEOPLASM OR NEOPLASMS)
L2         127 L1 AND (CANCER OR TUMOR OR NEOPLASM)

=> s l2 and py<=2003
      23975295 PY<=2003
L3          56 L2 AND PY<=2003
```

=> d l3 ibib abs 1-56

L3 ANSWER 1 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:107543 CAPLUS
DOCUMENT NUMBER: 140:252238
TITLE: Inhibition of indoleamine 2,3-dioxygenase suppresses NK cell activity and accelerates tumor growth
AUTHOR(S): Kai, Seiichiro; Goto, Shigeru; Tahara, Kouichirou; Sasaki, Atsushi; Kawano, Katsunori; Kitano, Seigo
CORPORATE SOURCE: Department of Surgery I, Oita University Faculty of Medicine, Oita, 897-5593, Japan
SOURCE: Journal of Experimental Therapeutics and Oncology (2003), 3(6), 336-345
CODEN: JETOFX; ISSN: 1359-4117
PUBLISHER: Blackwell Publishing, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Indoleamine 2,3-dioxygenase (IDO), a tryptophan catabolizing enzyme, is induced under various pathol. conditions, including viral and bacterial infection, allograft rejection, cerebral ischemia, and tumor growth. The authors have previously reported that the expression of IDO mRNA was increased in some clin. cases of hepatocellular carcinoma in which the recurrence-free survival rate in these IDO-pos. patients was higher than that in patients without IDO mRNA induction in tumors. Addnl., IDO expressed in tumors was localized not to the tumor cells but instead to tumor-infiltrating cells by immunohistochem. Here, to elucidate the mechanisms underlying anti-tumor effect of IDO, the authors investigated whether IDO inhibitor (1-methyl-DL-tryptophan, 1MT) affects the growth of s.c. B16 tumors in mice. Subsequently, the activity of natural killer (NK) cells was investigated under the conditions of inhibited IDO activity in vivo and in vitro. IDO mRNA expression of B16 cells, B16 s.c. tumor , splenocytes of mice, and human NK cells were studied by reverse transcription-polymerase chain reaction. B16 s.c. tumor growth with or without IDO inhibition was observed and cytotoxic activity of NK cells were investigated under the conditions of inhibited IDO activity in vivo and in vitro. IDO mRNA was expressed in B16 s.c. tumor, splenocytes of tumor bearing mice, co-cultured splenocytes with B16, and human NK cells. On day 14, after injection of B16 melanoma cells, the sizes of tumors in IDO-inhibited mice were larger than those in control mice. The cytotoxic activity of mouse NK cells was reduced by IDO inhibition in vivo. In in vitro inhibition of IDO, NK activity was reduced in dose-dependent manner of 1MT. Thus, IDO plays an important role in anti-tumor immunity by regulating cytotoxic activity of NK cells.
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:818069 CAPLUS
DOCUMENT NUMBER: 139:322295
TITLE: Antigen-presenting cell populations and their use as reagents for enhancing or reducing immune tolerance
INVENTOR(S): Mellor, Andrew L.; Munn, David H.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 36 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003194803	A1	20031016	US 2002-121909	20020412 <--
CA 2483451	A1	20031023	CA 2002-2483451	20020412 <--
WO 2003087347	A1	20031023	WO 2002-US11319	20020412 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002307243	A1	20031027	AU 2002-307243	20020412 <--
EP 1501918	A1	20050202	EP 2002-807233	20020412
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2006292618	A1	20061228	US 2006-474162	20060623
US 2007048769	A1	20070301	US 2006-474144	20060623

PRIORITY APPLN. INFO.: US 2002-121909 A 20020412
WO 2002-US11319 W 20020412

AB The disclosed invention is based on the discovery that antigen-presenting cells (APCs) may be generated to have predetd. levels of expression of the intracellular enzyme, indoleamine 2,3-dioxygenase (IDO). Because expression of high levels of IDO is correlated with a reduced ability to stimulate T cell responses and an enhanced ability to induce immunol. tolerance, APCs having high levels of IDO may be used to increase tolerance in the immune system, as for example in transplant therapy or treatment of autoimmune disorders. For example, APCs having high levels of IDO, and expressing or loaded with at least one antigen from a donor tissue may be used to increase tolerance of the recipient to the donor's tissue. Alternatively, APCs having reduced levels of IDO expression and expressing or loaded with at least one antigen from a cancer or infectious pathogen may be used as vaccines to promote T cell responses and increase immunity.

L3 ANSWER 3 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:764699 CAPLUS
DOCUMENT NUMBER: 139:322076
TITLE: Evidence for a tumoral immune resistance mechanism based on tryptophan degradation by indoleamine 2,3-dioxygenase
AUTHOR(S): Uyttenhove, Catherine; Pilotte, Luc; Theate, Ivan; Stroobant, Vincent; Colau, Didier; Parmentier, Nicolas; Boon, Thierry; Van den Eynde, Benoit J.
CORPORATE SOURCE: Ludwig Institute for Cancer Research and Cellular Genetics Unit, Universite de Louvain, Brussels, B-1200, Belg.
SOURCE: Nature Medicine (New York, NY, United States) (2003), 9(10), 1269-1274
CODEN: NAMEFI; ISSN: 1078-8956
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB T lymphocytes undergo proliferation arrest when exposed to tryptophan shortage, which can be provoked by indoleamine 2,3-dioxygenase (

IDO), an enzyme that is expressed in placenta and catalyzes tryptophan degradation Here we show that most human tumors constitutively express IDO. We also observed that expression of IDO by immunogenic mouse tumor cells prevents their rejection by preimmunized mice. This effect is accompanied by a lack of accumulation of specific T cells at the tumor site and can be partly reverted by systemic treatment of mice with an inhibitor of IDO, in the absence of noticeable toxicity. These results suggest that the efficacy of therapeutic vaccination of cancer patients might be improved by concomitant administration of an IDO inhibitor.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:669428 CAPLUS

DOCUMENT NUMBER: 139:290067

TITLE: Contribution of the MUC1 tandem repeat and cytoplasmic tail to invasive and metastatic properties of a pancreatic cancer cell line

AUTHOR(S): Kohlgraf, Karl G.; Gawron, Andrew J.; Higashi, Michiyo; Meza, Jane L.; Burdick, Michael D.; Kitajima, Shinichi; Kelly, David L.; Caffrey, Thomas C.; Hollingsworth, Michael A.

CORPORATE SOURCE: Department of Pathology and Microbiology, Eppley Institute for Research in Cancer and Allied Diseases, University of Nebraska Medical Center, Omaha, NE, 68198-6805, USA

SOURCE: Cancer Research (2003), 63(16), 5011-5020
CODEN: CNREA8; ISSN: 0008-5472

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB MUC1 is a polymorphic, highly glycosylated, type I transmembrane protein expressed by ductal epithelial cells of many organs including pancreas, breast, gastrointestinal tract, and airway. MUC1 is overexpressed and differentially glycosylated by adenocarcinomas that arise in these organs, and is believed to contribute to invasive and metastatic potential by contributing to cell surface adhesion properties [via the tandem repeat (TR) domain] and through morphogenetic signal transduction via the cytoplasmic tail (CT). The large extracellular TR of MUC1 consists of a heavily glycosylated, 20 amino acid sequence that shows allelic variation with respect to number of repeats. This portion of MUC1 may directly mediate adhesive or antiadhesive interactions with other surface mols. on adjacent cells and through these interactions initiate signal transduction pathways that are transmitted through the CT. We investigated the contribution of the TR domain and the CT of MUC1 to the in vivo invasive and metastatic potential, and the gene expression profile of the human pancreatic tumor cell line S2-013. Results showed that S2-013 cells overexpressing full-length MUC1 displayed a less invasive and metastatic phenotype compared with control-transfected cells and cells expressing MUC1 lacking the TR domain or CT. Clonal populations were analyzed by cDNA array gene expression anal., which showed differences in the gene expression profiles between the different cell lines. Among the genes differentially expressed were several that encode proteins believed to play a role in invasion and metastasis.

REFERENCE COUNT: 79 THERE ARE 79 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:491063 CAPLUS

DOCUMENT NUMBER: 139:57897

TITLE: Novel pharmaceutical composition of interferon gamma or pirfenidone combined with molecular diagnostics for the improved treatment of interstitial lung diseases
INVENTOR(S): Bevec, Dorian; Ziesche, Rolf
PATENT ASSIGNEE(S): Mondobiotech SA, Switz.
SOURCE: PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003051388	A2	20030626	WO 2002-CH691	20021212 <--
WO 2003051388	A3	20031030		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2470763	A1	20030626	CA 2002-2470763	20021212 <--
AU 2002347182	A1	20030630	AU 2002-347182	20021212 <--
BR 2002007310	A	20040817	BR 2002-7310	20021212
EP 1455813	A2	20040915	EP 2002-782602	20021212
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
CN 1620309	A	20050525	CN 2002-828206	20021212
JP 2005528082	T	20050922	JP 2003-552321	20021212
NO 2003003642	A	20031017	NO 2003-3642	20030815 <--
US 2006270618	A1	20061130	US 2004-498079	20040608
IN 2004DN07852	A	20070427	IN 2004-DN7852	20040615
IN 2004DN01679	A	20070525	IN 2004-DN1679	20040615
PRIORITY APPLN. INFO.:			EP 2001-130011 A	20011218
			WO 2002-CH691 W	20021212

AB The present invention relates to a novel pharmaceutical composition of compds. having the biol. activity of interferon gamma (IFN-γ) or pirfenidone in combination with a diagnostic array of candidate polynucleotides for the improved treatment of all forms of interstitial lung diseases, in particular of idiopathic pulmonary fibrosis (IPF). This invention describes the combination of mol. diagnosis and clin. therapy as a novel medication principle for reduction of mortality and improvement of disease management in interstitial lung diseases.

L3 ANSWER 6 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:355709 CAPLUS
DOCUMENT NUMBER: 138:335902
TITLE: Nucleic acid molecules and proteins for the identification, assessment, prevention, and therapy of ovarian cancer
INVENTOR(S): Monahan, John E.; Gannavarapu, Manjula; Hoersch, Sebastian; Kamatkar, Shubhangi; Kovats, Steven G.; Meyers, Rachel E.; Morrisey, Michael P.; Olandt, Peter J.; Sen, Ami; Veiby, Petter Ole; Mills, Gordon B.; Bast, Robert C.; Lu, Karen; Schmandt, Rosemarie E.; Zhao, Xumei; Glatt, Karen
PATENT ASSIGNEE(S): Millennium Pharmaceuticals, Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 44 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003087250	A1	20030508	US 2002-97340	20020314 <--
WO 2002071928	A2	20020919	WO 2002-US7826	20020314 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002258518	A1	20020924	AU 2002-258518	20020314 <--
US 2005214831	A1	20050929	US 2005-50926	20050204

PRIORITY APPLN. INFO.:		
US 2001-276025P	P	20010314
US 2001-276026P	P	20010314
US 2001-311732P	P	20010810
US 2001-323580P	P	20010919
US 2001-324967P	P	20010926
US 2001-325102P	P	20010926
US 2001-325149P	P	20010926
US 2002-97340	A1	20020314
WO 2002-US7826	W	20020314

AB The invention relates to newly discovered nucleic acid mols. and proteins associated with ovarian cancer. All OV markers and M352-M360 markers were identified by transcriptional profiling using mRNA from 9 normal ovarian epithelia, 11 stage I/II ovarian cancer tumors, and 25 stage III/IV tumors. Clones having expression ≥2-fold higher in ovarian tumors as compared to their expression in non-ovarian tumor tissues in at least 4 tumor samples were selected. Addnl. Mxxx markers were identified by transcriptional profiling using mRNA from 67 ovarian tumors of various histotypes and stage and 96 non-ovarian tumor tissues including normal ovarian epithelium, benign conditions, other normal tissues, and other abnormal tissues. Clones having expression ≥3-fold higher in at least 10% of ovarian tumors, as compared to their expression in non-ovarian tumor tissue, were designated as ovarian cancer specific markers. Clones were identified by BLAST anal., against both public and proprietary sequence databases, of EST sequences known to be associated with each clone. A total of 363 cDNA markers including their protein products are provided. Compns., kits, and methods for detecting, characterizing, preventing, and treating human ovarian cancers are provided.

L3 ANSWER 7 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:968965 CAPLUS
DOCUMENT NUMBER: 138:88595
TITLE: Tryptophan deprivation sensitizes activated T cells to apoptosis prior to cell division
AUTHOR(S): Lee, Geon Kook; Park, Hyeon Jin; MacLeod, Megan; Chandler, Phillip; Munn, David H.; Mellor, Andrew L.
CORPORATE SOURCE: Program in Molecular Immunology, Institute of Molecular Medicine and Genetics, Medical College of

Georgia, Augusta, GA, 30912, USA
SOURCE: Immunology (2002), 107(4), 452-460
CODEN: IMMUAM; ISSN: 0019-2805
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cells expressing indoleamine 2,3-dioxygenase (IDO), an enzyme which catabolizes tryptophan, prevent T-cell proliferation in vitro, suppress maternal anti-fetal immunity during pregnancy and inhibit T-cell-mediated responses to tumor-associated antigens. To examine the mechanistic basis of these phenomena the authors activated naive murine T cells in chemical defined tryptophan-free media. Under these conditions T cells expressed CD25 and CD69 and progressed through the first 12 h of G0/G1 phase but did not express CD71, cyclin D3, cdk4, begin DNA synthesis, or differentiate into cytotoxic effector cells. In addition, activated T cells with their growth arrested by tryptophan deprivation exhibited enhanced tendencies to die via apoptosis when exposed to anti-Fas antibodies. Apoptosis was inhibited by caspase inhibitor and was not observed when T cells originated from Fas-deficient mice. These findings suggest that T cells activated in the absence of free tryptophan entered the cell cycle but cell cycle progression ceased in mid-G1 phase and T cells became susceptible to death via apoptosis, in part though Fas-mediated signaling. Thus, mature antigen-presenting cells expressing IDO and Fas-ligand may induce antigen-specific T-cell tolerance by blocking T-cell cycle progression and by rapid induction of T-cell activation induced cell death in local tissue microenvironments.
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:787505 CAPLUS
DOCUMENT NUMBER: 138:105164
TITLE: Indolamine 2,3-dioxygenase, immunosuppression and pregnancy
AUTHOR(S): Mellor, Andrew L.; Chandler, Phillip; Lee, Geon Kook; Johnson, Theodore; Keskin, Derin B.; Lee, Jeffrey; Munn, David H.
CORPORATE SOURCE: Institute of Molecular Medicine and Genetics, Program in Molecular Immunology, Medical College of Georgia, Augusta, GA, 30912, USA
SOURCE: Journal of Reproductive Immunology (2002), 57(1-2), 143-150
CODEN: JRIMDR; ISSN: 0165-0378
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Pharmacol. inhibition of indolamine 2,3-dioxygenase (IDO) activity during murine pregnancy results in maternal T-cell-mediated rejection of allogeneic but not syngeneic conceptuses. Increased risk of allogeneic pregnancy failure induced by exposure to IDO inhibitor is strongly correlated with maternal C3 deposition at the maternal-fetal interface. Here we review evidence that cells expressing IDO contribute to immunosuppression by inhibiting T-cell responses to tumor antigens and tissue allografts, as well as fetal tissues.
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 9 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:674702 CAPLUS
DOCUMENT NUMBER: 137:200238
TITLE: Indoleamine 2,3-dioxygenase contributes to

tumor cell evasion of T cell-mediated rejection

AUTHOR(S): Friberg, Maria; Jennings, Ronald; Alsarraj, Marwan; Dessureault, Sophie; Cantor, Alan; Extermann, Martine; Mellor, Andrew L.; Munn, David H.; Antonia, Scott J.

CORPORATE SOURCE: Department of Interdisciplinary Oncology, H. Lee Moffitt Cancer Center, Tampa, FL, 33612, USA

SOURCE: International Journal of Cancer (2002), 101(2), 151-155
CODEN: IJCNAW; ISSN: 0020-7136

PUBLISHER: Wiley-Liss, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The priming of an appropriate antitumor T cell response rarely results in the rejection of established tumors. The characteristics of tumors that allow them to evade a T cell-mediated rejection are unknown for many tumors. The authors report on evidence that the expression of the immunosuppressive enzyme, indoleamine 2,3-dioxygenase (IDO) by mononuclear cells that invade tumors and tumor-draining lymph nodes, is a mechanism that may account for this observation. Lewis lung carcinoma (LLC) cells stimulated a more robust allogeneic T cell response in vitro in the presence of a competitive inhibitor of IDO, I-Me tryptophan. When administered in vivo this inhibitor also resulted in delayed LLC tumor growth in syngeneic mice. The authors' study provides evidence for a novel mechanism whereby tumors evade rejection by the immune system, and suggests the possibility that inhibiting IDO may be developed as an anti-cancer immunotherapeutic strategy.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 10 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:57331 CAPLUS

DOCUMENT NUMBER: 136:319540

TITLE: Gene profiling reveals unknown enhancing and suppressive actions of glucocorticoids on immune cells

AUTHOR(S): Galon, Jerome; Franchimont, Denis; Hiroi, Naoki; Frey, Gregory; Boettner, Antje; Ehrhart-Bornstein, Monika; O'Shea, John J.; Chrousos, George P.; Bornstein, Stefan R.

CORPORATE SOURCE: Lymphocyte Cell Biology Section, NIAMS, National Institutes of Health, Bethesda, MD, 20892, USA

SOURCE: FASEB Journal (2002), 16(1), 61-71
CODEN: FAJOEC; ISSN: 0892-6638

PUBLISHER: Federation of American Societies for Experimental Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Glucocorticoids continue to be the major immunomodulatory agents used in clin. medicine today. However, their actions as anti-inflammatory and immunosuppressive drugs are both beneficial and deleterious. We analyzed the effect of glucocorticoids on the gene expression profile of peripheral blood mononuclear cells from healthy donors. DNA microarray anal. combined with quant. TaqMan PCR and flow cytometry revealed that glucocorticoids induced the expression of chemokine, cytokine, and complement family members as well as of newly discovered innate immune-related genes, including scavenger and Toll-like receptors. In contrast, glucocorticoids repressed the expression of adaptive immune-related genes. Simultaneous inhibitory and stimulatory effects of glucocorticoids were found on inflammatory T helper subsets and apoptosis-related gene clusters. In cells activated by T cell receptor

crosslinking, glucocorticoids down-regulated the expression of specific genes that were previously up-regulated in resting cells, suggesting a potential new mechanism by which they exert pos. and neg. effects. Considering the broad and continuously renewed interest in glucocorticoid therapy, the profiles we describe here will be useful in designing more specific and efficient treatment strategies.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 11 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:835010 CAPLUS

DOCUMENT NUMBER: 136:16482

TITLE: Norharman, an indoleamine-derived β-carboline, but not Trp-P-2, a γ-carboline, induces apoptotic cell death in human neuroblastoma SH-SY5Y cells

AUTHOR(S): Uezono, T.; Maruyama, W.; Matsubara, K.; Naoi, M.; Shimizu, K.; Saito, O.; Ogawa, K.; Mizukami, H.; Hayase, N.; Shiono, H.

CORPORATE SOURCE: Department of Legal Medicine, Asahikawa Medical College, Asahikawa, Japan

SOURCE: Journal of Neural Transmission (2001), 108(8-9), 943-953
CODEN: JNTRF3; ISSN: 1435-1463

PUBLISHER: Springer-Verlag Wien

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Carbolines, azaheterocyclic amines derived from indoleamines, have various biol. activities, such as neurotoxicity of β-carbolines and potent mutagenicity of γ-carbolines. In this study, structural significance among these carbolines was investigated in relation to the types of cell death, apoptosis and necrosis, using human neuroblastoma SH-SY5Y cells. DNA damage was quant. analyzed by a single-cell gel electrophoresis assay. DNA damage was induced by both β-carbolines, harman and norharman, and γ-carbolines, 3-amino-1,4-dimethyl-5H-pyrido[4,3-b]indole (Trp-P-1) and 3-amino-4-methyl-5H-pyrido[4,3-b]indole (Trp-P-2), in a dose dependent manner. γ-Carbolines were more potent to damage DNA than β-carbolines. Alkaline lysis of the cells prevented DNA damage induced by β-carboline, and pre-treatment of the cells with cycloheximide, an inhibitor of protein synthesis, reduced DNA damage caused by norharman. Morphol. observation showed condensed and fragmented nuclei typical for apoptosis, in the cells treated with norharman. Thus, DNA damage induced by norharman was proved to be apoptotic. However, harman, which had a Me substitution at the position 1, might induce necrosis in the cells. On the other hand, γ-carbolines, Trp-P-1 and Trp-P-2, directly damaged DNA. Thus, the nitrogen atom at the γ-position and/or an amino group in carboline structure would be required to induce the direct DNA cleavage.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 12 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:796060 CAPLUS

DOCUMENT NUMBER: 136:132926

TITLE: Synthesis and release of neurotoxic kynurenine metabolites by human monocyte-derived macrophages

AUTHOR(S): Chiarugi, Alberto; Calvani, Maura; Meli, Elena; Traggiai, Elisabetta; Moroni, Flavio

CORPORATE SOURCE: Department of Preclinical and Clinical Pharmacology, University of Florence, Florence, 50139, Italy

SOURCE: Journal of Neuroimmunology (2001), 120(1-2), 190-198

CODEN: JNRIDW; ISSN: 0165-5728
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors studied the regulation of the kynurenine pathway of tryptophan metabolism in human monocyte-derived macrophages (MDM) with the aim of evaluating macrophage involvement in inflammatory neurol. disorders. Cultured MDM metabolized tryptophan and released kynurenine metabolites, including the excitotoxin quinolinic acid (QUIN). Lipopolysaccharides (LPS) or the pro-inflammatory cytokines INFγ and TNFα increased, while IL 4 or IL 10 inhibited the rate of tryptophan metabolism and the release of QUIN. The incubation media of INFγ-exposed MDM caused neuronal death in primary cultures of mixed cortical cells. Glutamate receptor antagonists or poly(ADP-ribose) polymerase inhibitors significantly reduced this death, thus suggesting new possibilities for the treatment of neuronal damage in neuroinflammatory disorders.
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 13 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:411495 CAPLUS
DOCUMENT NUMBER: 135:179631
TITLE: Profiling changes in gene expression during differentiation and maturation of monocyte-derived dendritic cells using both oligonucleotide microarrays and proteomics
AUTHOR(S): Le Naour, Francois; Hohenkirk, Lyndon; Grolleau, Annabelle; Misek, David E.; Lescure, Pascal; Geiger, James D.; Hanash, Samir; Beretta, Laura
CORPORATE SOURCE: Department of Microbiology and Immunology, University of Michigan, Ann Arbor, MI, 48109-0666, USA
SOURCE: Journal of Biological Chemistry (2001), 276(21), 17920-17931
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Dendritic cells (DCs) are antigen-presenting cells that play a major role in initiating primary immune responses. The authors have utilized two independent approaches, DNA microarrays and proteomics, to analyze the expression profile of human CD14+ blood monocytes and their derived DCs. Anal. of gene expression changes at the RNA level using oligonucleotide microarrays complementary to 6300 human genes showed that .apprx.40% of the genes were expressed in DCs. A total of 255 genes (4%) were regulated during DC differentiation or maturation. Most of these genes were not previously associated with DCs and included genes encoding secreted proteins as well as genes involved in cell adhesion, signaling, and lipid metabolism Protein anal. of the same cell populations was done using two-dimensional gel electrophoresis. A total of 900 distinct protein spots were included, and 4% of them exhibited quant. changes during DC differentiation and maturation. Differentially expressed proteins were identified by mass spectrometry and found to represent proteins with Ca2+ binding, fatty acid binding, or chaperone activities as well as proteins involved in cell motility. In addition, proteomic anal. provided an assessment of post-translational modifications. The chaperone protein, calreticulin, was found to undergo cleavage, yielding a novel form. The combined oligonucleotide microarray and proteomic approaches have uncovered novel genes associated with DC differentiation and maturation and has allowed anal. of post-translational modifications of specific proteins as part of these processes.

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 14 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:790660 CAPLUS
DOCUMENT NUMBER: 133:349121
TITLE: Methods for increasing T cell proliferation
INVENTOR(S): Van, Den Eynde Benoit; Bilsborough, Janine; Boon-Falleur, Thierry
PATENT ASSIGNEE(S): Ludwig Institute for Cancer Research, USA
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000066764	A1	20001109	WO 2000-US12118	20000503 <--
W: AU, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1185687	A1	20020313	EP 2000-928796	20000503 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1999-132219P P 19990503
WO 2000-US12118 W 20000503

AB The invention provides methods and compns. for increasing T cell proliferation using tryptophan enhancing agents. T cell proliferation can be increased in vitro by addition of tryptophan enhancing agents to T cell culture, or in vivo by administration of tryptophan enhancing agents. Also provided are methods for diagnosing and treating disorders characterized by constitutive expression of indoleamine -2,3-dioxygenase. Compns. and apparatus relating to the methods also are provided.
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 15 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:670740 CAPLUS
DOCUMENT NUMBER: 134:157226
TITLE: Parallel decrease in neurotoxin quinolinic acid and soluble tumor necrosis factor receptor p75 in serum during highly active antiretroviral therapy of HIV type 1 disease
AUTHOR(S): Look, Markus P.; Altfeld, Markus; Kreuzer, Karl A.; Riezler, Rainer; Stabler, Sally P.; Allen, Robert H.; Sauerbruch, Tilman; Rockstroh, Jurgen K.
CORPORATE SOURCE: Department of General Internal Medicine, University of Bonn, Bonn, 53105, Germany
SOURCE: AIDS Research and Human Retroviruses (2000), 16(13), 1215-1221
CODEN: ARHRE7; ISSN: 0889-2229
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The chronic immune activation state in HIV disease leads to increased activity of the rate-limiting tryptophan-kynurenine pathway enzyme indoleamine 2,3-dioxygenase (2,3-IDO), thereby increasing the formation of neurotoxic tryptophan metabolites such as kynurenine and quinolinic acid. We investigated whether highly active

antiretroviral therapy (HAART) (median duration, 100 days; range, 50-188 days) lowers serum levels of these metabolites in HIV-infected individuals and if so, whether this was paralleled by changes in a surrogate marker for immune activation, i.e., soluble tumor necrosis factor receptor p75 (sTNFR p75) concns. Baseline quinolinic acid (848 nM, 95% CI 567-1130 vs. 303 nM, 95% CI 267.1-339.5) and kynurenine (4.1 μM, 95% CI 3.3-4.9 vs. 2.7 μM, 95% CI 2.4-2.9) concns. as well as the mean kynurenine-to-tryptophan ratio (108.2, 95% CI 76.1-140.4 vs. 51.4, 95% CI 47.6-55.3) in 17 HIV-1-infected outpatients (7 with AIDS) were significantly higher than those in 55 healthy age-matched controls ($p < 0.01$), resp. Serum quinolinic acid concns. in 14 of 17 patients decreased (mean, -44.4%) during HAART in comparison with baseline (471.2 nM, 95% CI 288-654.3; $p = 0.022$). Thirteen of these 14 patients also had decreases in sTNFR p75 concns. Overall, the mean sTNFR p75 concentration decreased by 36.3% (13.5 ng/mL, 95% CI 9.3-17.8 vs. 8.6 ng/mL, 95% CI 5.9-11.4; $p = 0.01$, $n = 17$). Reduction in viral load through HAART and subsequent mitigation of the pathol. immune activation state in HIV disease may have reduced 2,3-IDO over activation. This eventually led to a decrease in quinolinic acid formation. The parallel reduction of the immune activation marker sTNFR p75 supports this hypothesis.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 16 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:615616 CAPLUS

DOCUMENT NUMBER: 134:188864

TITLE: Maturation of Human Monocyte-Derived Dendritic Cells Studied by Microarray Hybridization

AUTHOR(S): Dietz, Allan B.; Bulur, Peggy A.; Knutson, Gaylord J.; Matasic, Richard; Vuk-Pavlovic, Stanimir

CORPORATE SOURCE: Stem Cell Laboratory, Mayo Clinic Cancer Center, Mayo Clinic, Rochester, MN, 55905, USA

SOURCE: Biochemical and Biophysical Research Communications (2000), 275(3), 731-738
CODEN: BBRCA9; ISSN: 0006-291X

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We compared the transcript profiles of human myeloid immature dendritic (IDC) cells and mature dendritic cells (MDC) by hybridization of cell-derived cDNA to DNA probes immobilized on microarrays. The microarrays contained probes for 4110 known genes. We report maturation-dependent changes in transcription of clusters of differentiation, cytokines, cytokine receptors, chemokines, chemokine receptors, neuropeptides, adhesion mols., and other genes. We identified 1124 transcripts expressed in IDC and 1556 transcripts expressed in MDC. Maturation increased the levels of 291 transcripts twofold or more and reduced the levels of 78 transcripts to one-half or less than in IDC. We identified a concerted maturation-stage-dependent transcription of the variable chains of the members of the γ-chain-cytokine receptor family IL-4R, IL-7R, and IL-15R. Also, we found the reversal of the ratio of transcripts for galectin-3 and galectin-9 upon maturation. We identified maturation-dependent changes in the levels of transcripts for numerous genes encoding proteins previously undetected in dendritic cells such as indoleamine 2,3-deoxygenase, Epstein-Barr virus induced protein 3 and kinesin-2. Moreover, MDC transcribed and translated insulin like growth factor-1 receptor, transforming growth factor α, and neuropeptide Y. Full exptl. details are described in the electronic version of this paper available at http://www.mayo.edu/research/vuk_lab/.

REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 17 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:403419 CAPLUS
DOCUMENT NUMBER: 133:129960
TITLE: Melatonin, experimental basis for a possible application in breast cancer prevention and treatment
AUTHOR(S): Cos, S.; Sanchez-Barcelo, E. J.
CORPORATE SOURCE: Department of Physiology and Pharmacology, University of Cantabria, Santander, 39011, Spain
SOURCE: Histology and Histopathology (2000), 15(2), 637-647
CODEN: HIHIES; ISSN: 0213-3911
PUBLISHER: Histology and Histopathology
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with .apprx.120 refs. The role of the pineal as an oncostatic gland has been studied in animal models of tumorigenesis, especially on those concerning the mammary gland. The general conclusion is that exptl. manipulations activating pineal gland, or the administration of melatonin, reduce the incidence and growth rate of chemical-induced murine mammary tumors, while pinealectomy or situations which implicate a reduction of melatonin production usually stimulate mammary carcinogenesis. The direct actions of melatonin on mammary tumors have been suggested because of its ability to inhibit, at physiol. doses (1nM), the in vitro proliferation of MCF-7 human breast cancer cells. In this article we review the outstanding findings related to melatonin actions on mammary which, taken together, support a possible usefulness of this indoleamine in the prevention and treatment of mammary gland malignancy.
REFERENCE COUNT: 105 THERE ARE 105 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 18 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:152116 CAPLUS
DOCUMENT NUMBER: 133:53257
TITLE: Inhibition of tumor growth by L-deprenyl involves neural-immune interactions in rats with spontaneously developing mammary tumors
AUTHOR(S): Thyagarajan, Srinivasan; Madden, Kelley S.; Stevens, Suzanne Y.; Felten, David L.
CORPORATE SOURCE: Center for Neuroimmunology, Loma Linda University School of Medicine, Loma Linda, CA, 92350, USA
SOURCE: Anticancer Research (1999), 19(6B), 5023-5028
CODEN: ANTRD4; ISSN: 0250-7005
PUBLISHER: International Institute of Anticancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB L-deprenyl, a monoamine oxidase-B inhibitor, has been shown to reverse the age-related decline in sympathetic noradrenergic innervation and immune function in old rats and enhance T cell and NK cell activity in tumor-bearing rats. The objective of the present study was to examine whether deprenyl treatment of old female rats with mammary tumors could augment sympathetic nervous system and immune responses to inhibit the tumor growth. Female Sprague-Dawley rats with spontaneous mammary tumors were administered 0, 2.5 mg, or 5.0 mg/kg body weight (BW)/day deprenyl for i.p. 9 wk. Tumor diameter, tumor number and body weight were measured throughout the treatment period. At the end of the treatment period, norepinephrine (NE) concentration, interferon-γ production (IFN-γ), Con A-induced T

lymphocyte proliferation, and percentage of T and B lymphocytes and natural killer cells were measured in the spleen, and the concns. of monoamines were measured in the medial basal hypothalamus. Relative to saline-treated controls, treatment with deprenyl reduced tumor growth, increased NE concentration, IFN-γ production and percentage of the CD8+ T lymphocytes in the spleen. In the medial basal hypothalamus, deprenyl treatment increased the concns. of catecholamines and indoleamine . These results suggest that the anti-tumor effects of deprenyl on spontaneous rat mammary tumors may be achieved via neural-immune signaling in the spleen and medial basal hypothalamus.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 19 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:145067 CAPLUS
DOCUMENT NUMBER: 132:206569
TITLE: Expression monitoring for human cytomegalovirus (HCMV) infection, and genes possibly involved in mediating the pathology of HCMV infection
INVENTOR(S): Zhu, Hua; Gingeras, Thomas; Shenk, Thomas
PATENT ASSIGNEE(S): Affymetrix, Inc., USA
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000011218	A1	20000302	WO 1999-US18772	19990820 <--
WO 2000011218	A9	20020829		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9956776	A1	20000314	AU 1999-56776	19990820 <--
PRIORITY APPLN. INFO.:			US 1998-97708P P	19980821
			WO 1999-US18772 W	19990820

AB The invention provides methods, compns., and apparatus for studying the complex regulatory relationships among host genes and viruses, in particular HCMV. The invention also provides cellular mRNAs whose levels change by a factor of four or more after infection with HCMV. Such genes are likely those involved in mediating the pathol. of the infected tissues. Thus by identifying agents which are able to reverse the induction or repression of such genes, one can find candidate therapeutic agents for use in treating and or preventing HCMV-caused disease pathologies.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 20 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1999:527609 CAPLUS
DOCUMENT NUMBER: 131:266696
TITLE: L-Deprenyl inhibits tumor growth, reduces serum prolactin, and suppresses brain monoamine metabolism in rats with carcinogen-induced mammary tumors

AUTHOR(S): ThyagaRajan, Srinivasan; Quadri, S. Kaleem
CORPORATE SOURCE: Neuroendocrine Research Laboratory, Kansas State University, Manhattan, KS, USA
SOURCE: Endocrine (1999), 10(3), 225-232
CODEN: EOCRE5; ISSN: 1355-008X
PUBLISHER: Humana Press Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Previously, we have reported that L-deprenyl decreased the incidence of mammary tumors and pituitary tumors in old acyclic rats. The objective of the present study was to investigate the effects of L-deprenyl, a monoamine oxidase-B (MAO-B) inhibitor, treatment on the development and growth of tumors and on the metabolism of catecholamines and indoleamine in the medial basal hypothalamus (MBH) and the striatum (ST) of rats bearing 7, 12-dimethylbenzanthracene (DMBA)-induced mammary tumors. Female Sprague-Dawley rats with DMBA-induced mammary tumors were injected (s.c.) daily with 0.25 mg or 5.0 mg of deprenyl/kg BW or the vehicle (saline; control) for 12 wk. Tumor diameter, tumor number, body weight, and feed intake were measured every week of the treatment period. Serum PRL and the concns. of catecholamines, indoleamine , and their metabolites were measured by RIA and HPLC, resp. Treatment with 5.0 mg deprenyl decreased the tumor diameter, tumor number, and serum prolactin (PRL) level. Although the body weight increased in all three groups, the body weight gain in the 5.0 mg group was smaller than that in the control and 0.25 mg groups. Deprenyl treatment had no effect on feed intake. The concns. of dihydroxyphenylacetic acid (DOPAC) and homovanillic acid (HVA) were decreased in the MBH and the ST, and the concentration of 5-hydroxyindoleacetic acid (5-HIAA) was decreased in the MBH of deprenyl-treated rats. Treatment with 5.0 mg deprenyl enhanced the concns. of norepinephrine (NE) and serotonin (5-HT) in the MBH and in the ST, and the concentration of dopamine (DA) in the MBH. These results suggest that the suppression of the development and growth of DMBA-induced mammary tumors by chronic deprenyl treatment may be mediated through alterations in the synthesis and metabolism of catecholamines and indoleamine in the MBH and inhibition of PRL secretion.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 21 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:388082 CAPLUS
DOCUMENT NUMBER: 131:35866
TITLE: Regulation of T cell-mediated immunity by tryptophan
INVENTOR(S): Munn, David; Mellor, Andrew
PATENT ASSIGNEE(S): Medical College of Georgia Research Institute, Inc., USA
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9929310	A2	19990617	WO 1998-US25840	19981204 <--
WO 9929310	A3	20000106		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,

UA, UG, UZ, VN, YU, ZW
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9916285	A	19990628	AU 1999-16285	19981204	<--
US 6395876	B1	20020528	US 1998-205939	19981204	<--
US 6451840	B1	20020917	US 1998-206274	19981204	<--
US 2001001040	A1	20010510	US 2000-727055	20001130	<--
US 6482416	B2	20021119			
US 2002155104	A1	20021024	US 2002-112362	20020328	<--
US 7160539	B2	20070109			
US 2007077224	A1	20070405	US 2006-602930	20061121	
US 2007077234	A1	20070405	US 2006-603291	20061121	

PRIORITY APPLN. INFO.:

US 1997-67610P	P	19971205
US 1998-80380P	P	19980401
US 1998-80384P	P	19980401
US 1998-206274	A3	19981204
WO 1998-US25840	W	19981204
US 2002-112362	A3	20020328

AB A mechanism of macrophage-induced T cell suppression is the selective elimination of tryptophan and/or increase in one or more tryptophan metabolites within the local macrophage microenvironment. Studies demonstrate that expression of IDO (indoleamine 2,3-dioxygenase) can serve as a marker of suppression of T cell activation, and may play a significant role in allogeneic pregnancy and therefore other types of transplantation, and that inhibitors of IDO can be used to activate T cells and therefore enhance T cell activation when the T cells are suppressed by pregnancy, malignancy or a virus such as HIV. Inhibiting tryptophan degradation (and thereby increasing tryptophan concentration while decreasing tryptophan metabolite concentration), or supplementing tryptophan concentration, can therefore be used in addition to, or in place of, inhibitors of IDO. Similarly, increasing tryptophan degradation (thereby, decreasing tryptophan concentration and increasing tryptophan metabolite concentration), for example, by increasing IDO concentration or IDO activity, can suppress T cells. Although described particularly with reference to IDO regulation, one can instead manipulate local tryptophan concns., and/or modulate the activity of the high affinity tryptophan transporter, and/or administer other tryptophan degrading enzymes. Regulation can be further manipulated using cytokines such as macrophage colony stimulating factor, interferon gamma, alone or in combination with antigen or other cytokines.

L3 ANSWER 22 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER:	1998:765634 CAPLUS
DOCUMENT NUMBER:	130:137555
TITLE:	Cellular gene expression altered by human cytomegalovirus: global monitoring with oligonucleotide arrays
AUTHOR(S):	Zhu, Hua; Cong, Jian-Ping; Mamtora, Gargi; Gingeras, Thomas; Shenk, Thomas
CORPORATE SOURCE:	Howard Hughes Medical Institute, Department of Molecular Biology, Princeton University, Princeton, NJ, 08544, USA
SOURCE:	Proceedings of the National Academy of Sciences of the United States of America (1998), 95(24), 14470-14475 CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER:	National Academy of Sciences
DOCUMENT TYPE:	Journal

LANGUAGE: English

AB Mechanistic insights to viral replication and pathogenesis generally have come from the anal. of viral gene products, either by studying their biochem. activities and interactions individually or by creating mutant viruses and analyzing their phenotype. Now it is possible to identify and catalog the host cell genes whose mRNA levels change in response to a pathogen. We have used DNA array technol. to monitor the level of ≈6,600 human mRNAs in uninfected as compared with human cytomegalovirus-infected cells. The level of 258 mRNAs changed by a factor of 4 or more before the onset of viral DNA replication. Several of these mRNAs encode gene products that might play key roles in virus-induced pathogenesis, identifying them as intriguing targets for further study.

REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 23 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1998:649638 CAPLUS

DOCUMENT NUMBER: 130:2998

TITLE: Effect of cytokines on growth of Toxoplasma gondii in murine astrocytes

AUTHOR(S): Halone, S. K.; Chiu, F.-C.; Weiss, L. M.

CORPORATE SOURCE: Department of Neurology, Albert Einstein College of Medicine, Bronx, NY, 10461, USA

SOURCE: Infection and Immunity (1998), 66(10), 4989-4993
CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Cytokines play a role in the regulation of T. gondii in the central nervous system. Cytokine-activated microglia are important host defense cells in central nervous system infections. Recent evidence indicates that astrocytes can also be activated by cytokines to inhibit intracellular pathogens. Here, the authors examined the effect of γ interferon (IFN-γ), tumor necrosis factor α (TNF-α), interleukin-6 (IL-6), and IL-1 on the growth of T. gondii in a primary murine astrocyte culture. Pretreatment of astrocytes with IFN-γ resulted in 65% inhibition of T. gondii growth. Neither TNF-α, IL-1, nor IL-6 alone had any effect on T. gondii growth. IFN-γ in combination with either TNF-α, IL-1, or IL-6 caused a 75-80% inhibition of growth. While nitric oxide was produced by astrocytes treated with these cytokines, inhibition of T. gondii growth was not reversed by the addition of the nitric oxide synthase inhibitor NG-monomethyl-L-arginine. Furthermore, IFN-γ in combination with IL-1, IL-6, or TNF-α also induced inhibition in astrocytes derived from syngeneic mice deficient in the enzyme inducible nitric oxide synthase. Apparently, the mechanism of cytokine inhibition is not nitric oxide mediated. Similarly, the addition of tryptophan had no effect on inhibition, indicating that the mechanism was not mediated via induction of the enzyme indoleamine 2,3-dioxygenase. The mechanism of inhibition remains to be elucidated. These results demonstrate that cytokine-activated astrocytes are capable of inhibiting the growth of T. gondii. Astrocytes may thus be important host defense cells in controlling toxoplasmosis in the brain.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 24 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1998:191552 CAPLUS

DOCUMENT NUMBER: 128:290477

TITLE: Melatonin enhances tamoxifen's ability to prevent the

reduction in microsomal membrane fluidity induced by lipid peroxidation

AUTHOR(S): Garcia, J. J.; Reiter, R. J.; Ortiz, G. G.; Oh, C. S.; Tang, L.; Yu, B. P.; Escames, G.

CORPORATE SOURCE: Department of Cellular and Structural Biology, University of Texas Health Science Center, San Antonio, TX, 78284, USA

SOURCE: Journal of Membrane Biology (1998), 162(1), 59-65
CODEN: JMBBBO; ISSN: 0022-2631

PUBLISHER: Springer-Verlag New York Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The indoleamine melatonin and the synthetic antiestrogenic drug tamoxifen seem to have similar mechanisms in inhibiting the growth of estrogen receptor pos. breast cancer cells. In this study, the authors compared the ability of these mols., alone and in combination, in stabilizing microsomal membranes against free radical attack. Hepatic microsomes were obtained from male rats and incubated with or without tamoxifen (50-200 FM), melatonin (1 mM) or both; lipid peroxidn. was induced by addition of FeCI3, NADPH and ADP. After oxidative damage, membrane fluidity, measured by fluorescence polarization techniques, decreased, whereas malonaldehyde (MDA) and 4-hydroxyalkenals (4-HDA) concns. increased. Incubation of the microsomes with tamoxifen prior to exposure to free radical generating processes inhibited, in a dose-dependent manner, the increase in membrane rigidity and the rise in MDA+4-HDA levels. When melatonin was added, the efficacy of tamoxifen in preventing membrane rigidity was enhanced. Thus, the IC50s for preventing membrane rigidity and for inhibiting lipid peroxidn. obtained for tamoxifen in the presence of melatonin were lower than those obtained with tamoxifen alone. Moreover, tamoxifen (50-200 μM) in the presence of melatonin reduced basal membrane fluidity and MDA+4-HDA levels in microsomes. These synergistic effects of tamoxifen and melatonin in stabilizing biol. membranes may be important in protecting membranes from free radical damage.

REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 25 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1998:72933 CAPLUS

DOCUMENT NUMBER: 128:225774

TITLE: Antitumor effect of l-deprenyl in rats with carcinogen-induced mammary tumors

AUTHOR(S): ThyagaRajan, Srinivasan; Felten, Suzanne Y.; Felten, David L.

CORPORATE SOURCE: Department of Neurobiology and Anatomy, University of Rochester School of Medicine, Rochester, USA

SOURCE: Cancer Letters (Shannon, Ireland) (1998), 123(2), 177-183
CODEN: CALEDQ; ISSN: 0304-3835

PUBLISHER: Elsevier Science Ireland Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Deprenyl, a monoamine oxidase-B (MAO-B) inhibitor, has a wide range of pharmacol. properties that are beneficial therapeutically in the treatment of human neurodegenerative diseases. Recent studies have demonstrated that deprenyl possesses a neuroprotective function that is not dependent on its MAO-B inhibitory activity. The focus of the present study was to investigate whether prolonged treatment of young Sprague-Dawley female rats with deprenyl before and after 9,10-dimethyl-1,2-benzanthracene (DMBA) administration would inhibit the development of mammary tumors by exerting a neuroprotective

effect on the tuberoinfundibular dopaminergic (TIDA) neurons in the medial basal hypothalamus (MBH). For this purpose, the concns. of catecholamines, indoleamine and their metabolites were measured in the MBH by high-performance liquid chromatog. (HPLC) at the end of the treatment period. Female Sprague-Dawley rats (28-29 days old) were treated i.p. with saline, or 0.25 or 2.5 mg of deprenyl/kg b.w. daily for 4 wk prior to the administration of DMBA. Following the administration of DMBA, the rats were treated with saline or deprenyl daily for 27 wk. At the end of the treatment period, there was a significant reduction in the tumor incidence and tumor number in rats that received 2.5 mg/kg deprenyl before and after the administration of DMBA and also in rats that were treated with 2.5 mg/kg deprenyl following DMBA. There also was a significant decrease in tumor number in rats that were treated with 0.25 mg/kg deprenyl during the entire treatment period of 31 wk. Body weight increased throughout the treatment period with no significant differences between the groups. Treatment of rats with 2.5 mg of deprenyl following the administration of DMBA and also during the entire treatment period resulted in a significant decrease in the concns. of the metabolites of norepinephrine (NE), dopamine (DA) and serotonin (5-HT) in the MBH, but there were no significant alterations in the concns. of NE, DA and 5-HT in the MBH. These results suggest that the administration of deprenyl blocked the development of mammary tumors in part by inhibiting the metabolism of catecholamines and indoleamine and possibly by conferring a neuroprotective effect on the TIDA neurons in the MBH, especially at 0.25 mg/kg of deprenyl.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 26 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1998:35862 CAPLUS

DOCUMENT NUMBER: 128:139599

TITLE: Multiple molecular and cellular changes associated with tumor stasis and regression during IL-12 therapy of a murine breast cancer model

AUTHOR(S): Dias, Sergio; Thomas, Hilary; Balkwill, Frances

CORPORATE SOURCE: Biological Therapies Laboratory, Imperial Cancer Research Fund, London, WC2A 3PX, UK

SOURCE: International Journal of Cancer (1998), 75(1), 151-157
CODEN: IJCNAW; ISSN: 0020-7136

PUBLISHER: Wiley-Liss, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB IL-12 treatment of a murine transplantable breast carcinoma (HTH-K) led to tumor regression and cure which was related to the duration of treatment. The authors studied the sequential mol. and phenotypic changes in IL-12-treated tumors. IFN-γ mRNA was detected 8 h after the first treatment. MRNA expression for the IFN-γ-inducible genes β2-microglobulin and indoleamine dioxygenase (IDO) was induced subsequently, together with the chemokine IP-10. IL-12-treated tumors had an abundant cellular infiltrate, consisting mainly of CD8+ T cells. MRNA for granzyme B and perforin also could be detected, suggesting that those cells were activated. After 7 days of daily therapy, tumors in IL-12-treated mice had a reduction in vasculature. Finally, the number of apoptotic tumor cells increased throughout IL-12 treatment. The authors compared the antitumor effects of IL-12 to those induced by IFN-γ therapy, which caused initial tumor stasis but subsequent tumor progression. IFN-γ induced β2-microglobulin and IDO over a 7-day period, but IP-10 was induced only transiently. IFN-γ caused a lesser cellular infiltrate, a minor anti-angiogenic effect, and a

transient apoptotic effect. The success of IL-12 may be due to its ability to produce a distinct sequence of mol. and phenotypic changes in tumors, leading to an antitumor immune response, toxicity against tumor cells, and an anti-angiogenic effect. Other cytokines, such as IFN-γ, induce some, but not all, of these actions. Comparison of IL-12 and IFN-γ suggests that sustained induction of IP-10 and activation of a resulting cellular infiltrate may be key changes in regressing tumors.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 27 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1996:694251 CAPLUS
DOCUMENT NUMBER: 125:326402
TITLE: An immunoreactive conjugate, method for its preparation, antibodies to the conjugate and a pharmaceutical composition and diagnostic device containing them
INVENTOR(S): Maes, Roland
PATENT ASSIGNEE(S): Anda Biologicals S.A., Fr.
SOURCE: Eur. Pat. Appl., 19 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
EP 736770	A2	19961009	EP 1996-870042		19960401	<--
EP 736770	A3	19970502				
R: BE, DE, FR, GB, IT						
BE 1009230	A6	19970107	BE 1995-316		19950405	<--
BE 1009917	A6	19971104	BE 1996-113		19960208	<--
PRIORITY APPLN. INFO.:			BE 1995-316	A	19950405	
			BE 1996-113	A	19960208	

AB An immunoreactive conjugate is disclosed which contains 1 or more haptens consisting of a sulfhydryl group and one of the following: amino acids, carbohydrates, amino carbohydrates, phosphatidylinositol, sphingosine, and their nitrosyl, acyl, or acetyl derivs., the haptens being coupled to a protein with a mol. weight >8000 Kd and/or a solid support by a coupling agent capable of binding to the sulfhydryl group of the hapten. Thus, NO-cysteine and NO-N-acetyl-L-cysteine conjugates with albumin were prepared, and birds and mammals were vaccinated. IgG and IgM class antibodies specific for N-acetyl-L-cysteine were detected in the subjects. Addnl. analyses demonstrated that many HIV-pos. patients have IgG specific for acetyl-cysteine. Pharmaceutical compns. using these immunoreactive conjugates can be used in the prevention and/or treatment of autoimmunity, AIDS, cancer, tuberculosis and a variety of other diseases.

L3 ANSWER 28 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1996:402922 CAPLUS
DOCUMENT NUMBER: 125:84214
TITLE: Molecular mechanisms underlying IFN-γ-mediated tumor growth inhibition induced during tumor immunotherapy with rIL-12
AUTHOR(S): Yu, Wen-Gong; Yamamoto, Norihiko; Takenaka, Hiroshi; Mu, Jie; Tai, Xu-Guang; Zou, Jian-Ping; Ogawa, Makoto; Tsutsui, Taeki; Wijesuriya, Rishani; et al.
CORPORATE SOURCE: Biomed. Res. Cent., Osaka Univ., Suita, 565, Japan
SOURCE: International Immunology (1996), 8(6), 855-865

CODEN: INIMEN; ISSN: 0953-8178
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The present study investigates the mol. mechanisms by which IFN-γ produced as a result of in vivo IL-12 administration exerts its anti-tumor effects. RIL-12 was administered 3 or 5 times into mice bearing CSA1M fibrosarcoma, OV-HM ovarian carcinoma, or MCH-1-A1 fibrosarcoma. This regimen induced complete regression of CSA1M and OV-HM tumors but only transient growth inhibition of MCH-1-A1 tumors. The anti-tumor effects of IL-12 were associated with enhanced induction of IFN-γ because these effects were abrogated by pretreatment of hosts with anti-IFN-γ antibody. Exposure in vitro of the 3 types of tumor cells to rIFN-γ resulted in moderate to potent inhibition of tumor cell growth. IFN-γ stimulated the expression of mRNAs for an inducible type of NO synthase (iNOS) in CSA1M cells and indoleamine 2,3-dioxygenase (IDO), an enzyme capable of degrading tryptophan, in OV-HM cells, but induced only marginal levels of these mRNAs in MCH-1-A1 cells. In association with iNOS gene expression, IFN-γ-stimulated CSA1M cells produced a large amount of NO which functioned to inhibit their own growth in vitro. Although OV-HM and MCH-1-A1 cells did not produce NO, they also exhibited NO susceptibility. Whereas the tumor masses from IL-12-treated CSA1M-bearing or OV-HM-bearing mice induced higher levels of iNOS (for CSA1M) or IDO and iNOS (for OV-HM) mRNAs, the MCH-1-A1 tumor mass expressed lower levels of iNOS mRNA alone. Moreover, massive infiltration of CD4+ and CD8+ T cells and Mac-1+ cells was seen only in the CSA1M and OV-HM tumors. Thus, IFN-γ produced after IL-12 treatment induces the expression of various genes with potential to modulate tumor cell growth by acting directly on tumor cells or stimulating tumor-infiltrating lymphoid cells and the effectiveness of IL-12 therapy is associated with the operation of these mechanisms.

L3 ANSWER 29 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1995:368434 CAPLUS
DOCUMENT NUMBER: 122:158241
TITLE: The role of indoleamine 2,3-dioxygenase in the anti-tumor activity of human interferon-γ in vivo
AUTHOR(S): Burke, Frances; Knowles, Richard G.; East, Nick; Balkwill, Frances R.
CORPORATE SOURCE: Biological Therapy Laboratory, Imperial Cancer Research Fund, London, WC2A 3PX, UK
SOURCE: International Journal of Cancer (1995), 60(1), 115-22
CODEN: IJCNAW; ISSN: 0020-7136
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors studied the relation between L-tryptophan metabolism and the response to human IFN-γ in 3 human ovarian cancer xenografts growing in nude mice. During IFN-γ therapy all 3 tumors showed a profound depletion in L-tryptophan and a corresponding rise in L-kynurenine. The microenvironment surrounding the tumors was also depleted of L-tryptophan. The IFN-γ-inducible enzyme indoleamine dioxygenase, IDO, was induced in treated tumors. While there was a variability in IDO mRNA expression in the different xenografts tested, in situ hybridization showed that the gene was induced at all levels of the tumor, and not just the periphery. Thus, induction of IDO by IFN-γ in vivo can metabolize L-tryptophan rapidly enough for it to become depleted, despite a continued

supply of L-tryptophan from the host. The IDO mRNA and protein remained induced after the L-tryptophan levels had returned to normal, suggesting that the gene may be post-transcriptionally regulated and/or the IDO co-factor supply may be limited. Another IFN-γ-inducible gene, tryptophanyl tRNA synthetase, was also induced in the tumor. It is possible that this enzyme, which is responsible for synthesizing tryptophanyl tRNA, acts in a compensatory manner by allowing protein synthesis to continue despite low free L-tryptophan concns. There was no correlation of the above parameters with the antitumor response to IFN-γ, suggesting that other mechanisms must play a role. L-Tryptophan depletion may be a contributor to a multifactorial growth inhibition of tumor cells following IFN-γ treatment, but cannot on its own explain their growth inhibition.

L3 ANSWER 30 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1993:647695 CAPLUS
DOCUMENT NUMBER: 119:247695
TITLE: Reversal of an interferon-γ-resistant phenotype by poly(I:C): Possible role of double-stranded RNA-activated kinase in interferon-γ signaling
AUTHOR(S): Ozes, Osman N.; Taylor, Milton W.
CORPORATE SOURCE: Dep. Biol., Indiana Univ., Bloomington, IN, 47405, USA
SOURCE: Journal of Interferon Research (1993), 13(4), 283-8
CODEN: JIREDJ; ISSN: 0197-8357
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Indoleamine 2,3-dioxygenase (IDO) is induced in neoplastic cell lines by interferon-γ (IFN-γ) treatment. In ME180 cervical carcinoma cells, there is a rapid increase in IDO mRNA accumulation beginning at 4 h after IFN-γ treatment and continuing for at least 24 h. The IFN-γ-resistant mutant of ME180, IR3B6B, expresses very low levels of IDO message after IFN-γ treatment. However, pretreatment of this mutant with poly(I:C) restores normal levels of IDO mRNAs and IDO enzyme activity. Poly(I:C) mediated reversal of the IFN-γ-resistant phenotype and induction of IDO mRNA are inhibited by 2-aminopurine. In vitro phosphorylation of calf thymus histone using the immunopptd. p68 kinase prepared from IFN-γ-treated ME180 and IR3B6B cells revealed the deficiency of activation of this kinase in IR3B6B cells after IFN-γ treatment, and treatment of this mutant cells with poly(I:C) restores p68 kinase activity. From these results, the authors conclude that a double-stranded RNA-dependent kinase is activated by IFN-γ treatment and its activation correlates with IFN-γ-mediated induction of the IDO gene.

L3 ANSWER 31 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1993:623991 CAPLUS
DOCUMENT NUMBER: 119:223991
TITLE: Induction of pterin synthesis is not required for cytokine-stimulated tryptophan metabolism
AUTHOR(S): Sakai, Naoki; Saito, Kuniaki; Kaufman, Seymour; Heyes, Melvyn P.; Milstien, Sheldon
CORPORATE SOURCE: Lab. Neurochem., Natl. Inst. Ment. Health, Bethesda, MD, 20892, USA
SOURCE: Biochemical Journal (1993), 295(2), 543-7
CODEN: BIJOAK; ISSN: 0306-3275
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Activation of the immune system which occurs in inflammatory diseases leads to parallel increases in pterin synthesis and increased production of

neuroactive L-tryptophan metabolites. Several model systems were studied to determine whether pterins, which are cofactors for hydroxylation reactions, could be required in the oxidative kynurenine pathway of L-tryptophan degradation Treatment of mice with interferon-γ increased L- tryptophan metabolism without any corresponding change in tissue biopterin concns. Cytokine-treated human fibroblasts, macrophages and glioblastoma cells all showed increases in kynurenine production, which were completely independent of pterin synthesis. When pterin synthesis de novo was blocked, either by an inhibitor of GTP cyclohydrolase or because of a genetic deficiency of one of the enzymes of the pathway of pterin biosynthesis, cytokine-stimulated increases in tryptophan metabolism were unaffected. Furthermore, increasing intracellular tetrahydrobiopterin concns. by treating cells with sepiapterin also had no effect on markers of tryptophan metabolism Therefore, both normal and cytokine-stimulated L-tryptophan metabolism appears to be completely independent of pterin biosynthesis.

L3 ANSWER 32 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1993:426374 CAPLUS
DOCUMENT NUMBER: 119:26374
TITLE: Induction of toxoplasmostasis in a human glioblastoma by interferon γ
AUTHOR(S): Daeubener, Walter; Pilz, Korinna; Zennati, Samira Seghrouchni; Bilzer, Thomas; Fischer, Hans Georg; Hadding, Ulrich
CORPORATE SOURCE: Inst. Med. Mikrobiol. Virol., Heinrich-Heine-Univ., Duesseldorf, D-4000, Germany
SOURCE: Journal of Neuroimmunology (1993), 43(1-2), 31-8
CODEN: JNRIDW; ISSN: 0165-5728
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In the course of human toxoplasmosis, central nervous system involvement often occurs. As a model for toxoplasma growth within human brain cells, the proliferation of Toxoplasma gondii strain BK within the human glioblastoma cell line 86HG39 was analyzed. The 86HG39 cells support the growth of toxoplasma similar to human monocyte derived macrophages and in contrast to human monocytes. The growth of T. gondii within interferon γ (IFNγ)-treated 86HG39 cells is reduced due to toxoplasmostasis and not due to toxoplasmocide effects. The mechanism of IFNγ-induced toxoplasmostasis was also investigated. IFNγ did not induce O2- production and/or nitrite oxide production, and inhibitors of O2- and NO2- did not influence IFNγ-induced toxoplasmostasis. In contrast, the supplementation of L-tryptophan to the culture medium completely abolished the IFNγ effect. Apparently, the induction of L-tryptophan degradation in 86HG39 cells by IFNγ, possibly by activation of the indoleamine-2,3-dioxygenase, is responsible for the IFNγ-induced toxoplasmostasis within the glioblastoma cell line.

L3 ANSWER 33 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1993:232062 CAPLUS
DOCUMENT NUMBER: 118:232062
TITLE: Tryptophan protects human melanoma cells against γ-interferon and tumor necrosis factor-α: a unifying mechanism of action
AUTHOR(S): Wood, J. M.; Ehrke, C.; Schallreuter, K. U.
CORPORATE SOURCE: Gray Freshwater Biol. Inst., Navarre, MN, 55392, USA
SOURCE: Melanoma Research (1991), 1(3), 177-85
CODEN: MREEEH; ISSN: 0960-8931
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The sensitivity and resistance of 6 human melanoma cell lines to

γ-interferon (γ-IFN) and tumor necrosis factor-α (TNF-α) were examined Amelanotic cell lines were more sensitive to γ-IFN and TNF-α than melanotic cells. The cytotoxicity of γ-IFN and TNF-α could be reversed in all cells by the addition of L- or D-tryptophan to the culture medium. Melanoma cells resistant to γ-IFN excrete Ca-activated neutral protease (CANP) and as a consequence, make L-tryptophan available by the hydrolysis of serum proteins in the culture medium. Resistance to γ-IFN could be reversed by the addition of specific CANP inhibitor, whereas γ-IFN-sensitive strains became more resistant with the addition of CANP to the culture medium. It has been confirmed that γ-IFN induces indoleamine 2,3-dioxygenase in melanoma cells. This enzyme utilizes the superoxide anion (O2-) as a substrate for the oxidation of either L- or D-tryptophan to N-formylkynurenine leading to cell death. The induction of this degradative pathway for L-tryptophan kills cells by starvation of this essential and relatively scarce amino acid. TNF-α induces Mn-containing superoxide dismutase (MnSOD) which also uses O2- to produce cytotoxic concns. of H2O2. Therefore, it can be concluded that the cytotoxicity of both γ-IFN and TNF-α depends on the availability of L-tryptophan as the substrate for the removal of O2- via indoleamine 2,3-dioxygenase.

L3 ANSWER 34 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1993:204906 CAPLUS
DOCUMENT NUMBER: 118:204906
TITLE: 4-Chloro-3-hydroxyanthranilate, 6-chlorotryptophan and norharmane attenuate quinolinic acid formation by interferon-γ-stimulated monocytes (THP-1 cells)
AUTHOR(S): Saito, Kuniaki; Chen, Cai Y.; Masana, Monica; Crowley, Jeffrey S.; Markey, Sanford P.; Heyes, Melvyn P.
CORPORATE SOURCE: Lab. Clin. Sci., Natl. Inst. Mental Health, Bethesda, MD, 20892, USA
SOURCE: Biochemical Journal (1993), 291(1), 11-14
CODEN: BIJOAK; ISSN: 0306-3275
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Accumulation of quinolinic acid and L-kynurenine occurs in the brain and/or blood following immune activation, and may derive from L-tryptophan following induction of indoleamine 2,3-dioxygenase and other kynurenine-pathway enzymes. In the present study a survey of various cell lines derived from either brain or systemic tissues showed that, while all cells examined responded to interferon-γ by increased conversion of L-[13C6]tryptophan into L-kynurenine (human: B-lymphocytes, neuroblastoma, glioblastoma, lung, liver, kidney; rat brain: microglia, astrocytes and oligodendrocytes), only macrophage-derived cells (peripheral-blood mononuclear cells; THP-1, U-937) and certain liver cells (SKHep1) synthesized [13C6]quniolinic acid. Tumor necrosis factor-α enhanced the effects of interferon-γ in THP-1 cells. Norharmane, 6-chloro-DL-tryptophan and 4-chloro-3-hydroxyanthranilate attenuated quinolinic acid formation by THP-1 cells with IC50 values of 51 μM, 58 μM and 0.11 μM resp. Norharmane and 6-chloro-DL-tryptophan attenuated L-kynurenine formation with IC50 values of 43 μM and 51 μM resp., whereas 4-chloro-3-hydroxyanthranilate had no effect on L-kynurenine accumulation. The redns. in L-kynurenine and quinolinic acid formation are consistent with the reports that norharmane is an inhibitor of indoleamine 2,3-dioxygenase, 6-chloro-DL-tryptophan is metabolized through the kynurenine pathway, and 4-chloro-3-hydroxyanthranilate is an inhibitor of 3-hydroxyanthranilate 3,4-dioxygenase. These results suggest that many tissues may contribute to the production of L-kynurenine following indoleamine 2,3-dioxygenase induction and immune activation. Quinolinic acid may be directly synthesized from L-tryptophan in both

macrophages and certain types of liver cells, although uptake of quinolinic acid precursors from blood may contribute to quinolinic acid synthesis in cells that cannot convert L-kynurenine into quinolinic acid.

L3 ANSWER 35 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1992:649764 CAPLUS
DOCUMENT NUMBER: 117:249764
TITLE: Differential induction of indoleamine -2,3-dioxygenase (IDO) by interferon-γ in human gynecologic cancer cells
AUTHOR(S): Leung, Benjamin S.; Stout, Lawrence E.; Shaskan, Edward G.; Thompson, Randall M.
CORPORATE SOURCE: Clin. Hosp., Univ. Minnesota, Minneapolis, MN, 55455, USA
SOURCE: Cancer Letters (Shannon, Ireland) (1992), 66(1), 77-81
CODEN: CALEDQ; ISSN: 0304-3835
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Induction of IDO by interferon-γ (IFN-γ) is thought to be a mechanism underlying the antineoplastic properties of IFN-γ. Since clin. trials with IFN-γ have yielded variable efficacy in treating cancers of gynecol. origin, the effects of IFN-γ on cell growth and IDO activity in cell lines from 7 gynecol. and 5 breast cancers were tested. At a dose of 250 IU/mL, IFN-γ suppressed cell growth and induced IDO activity in 1 cervical (C41), 1 vulva (A431), 1 breast (HS578T), and 2 ovarian (OVCAR-3, CAOV-3) cancer cell lines. Differing inhibition of cell growth, but with no induction of IDO activity, was found with IFN-γ treatment of the other cell lines.

L3 ANSWER 36 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1992:421185 CAPLUS
DOCUMENT NUMBER: 117:21185
TITLE: Regulation of T-cell proliferation via a novel 5HT1a receptor
INVENTOR(S): Aune, Thomas Martin
PATENT ASSIGNEE(S): Miles Inc., USA
SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9204015	A2	19920319	WO 1991-US6176		19910904 <--
WO 9204015	A3	19920416			
W: AU, CA, JP					
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE					
CA 2090688	A1	19920305	CA 1991-2090688		19910904 <--
CA 2090689	A1	19920305	CA 1991-2090689		19910904 <--
AU 9188482	A	19920330	AU 1991-88482		19910904 <--
EP 547172	A1	19930623	EP 1991-918533		19910904 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE					
JP 06503816	T	19940428	JP 1991-517820		19910904 <--
PRIORITY APPLN. INFO.:			US 1990-578710	A	19900904
			WO 1991-US6176	A	19910904

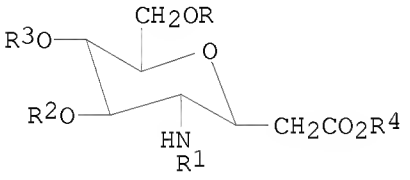
AB Methods of regulating proliferation or functions of activated T-cells exhibiting a 5HT1a receptor involve introducing a sufficient amount of agonists or antagonists to either increase or decrease T-cell

proliferation. The basis for regulating cell proliferation may be via (1) the 5HT1a receptor, (2) serotonin synthesis inhibition, and/or (3) serotonin stimulation of CD8+ subpopulations of activated T-cells. Methods of treating T-cell-dependent diseases, immune deficient diseases, and neoplastic diseases are also disclosed. The 5HT1a receptors on human Jurkat T-cells were studied; the receptors stimulated phosphatidylinositol turnover and increased intracellular Ca2+ concentration in these cells. Both CD4+ and CD8+ T-cells expressed elevated levels of the receptor. Serotonin slightly inhibited proliferation of T-cells in response to PHA but stimulated proliferation of T-cells in response to pokeweed mitogen by over 3-fold.

L3 ANSWER 37 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1992:236096 CAPLUS
DOCUMENT NUMBER: 116:236096
TITLE: Preparation of 2,4-dideoxy-4,5,6-triacyl-glycero-ido-octonic acids as immunological adjuvants
INVENTOR(S): Vyplel, Hermann
PATENT ASSIGNEE(S): Sandoz-Patent-G.m.b.H., Germany
SOURCE: Ger. Offen., 8 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4028680	A1	19920312	DE 1990-4028680	19900910 <--
PRIORITY APPLN. INFO.:			DE 1990-4028680	19900910

OTHER SOURCE(S): CASREACT 116:236096; MARPAT 116:236096
GI



I

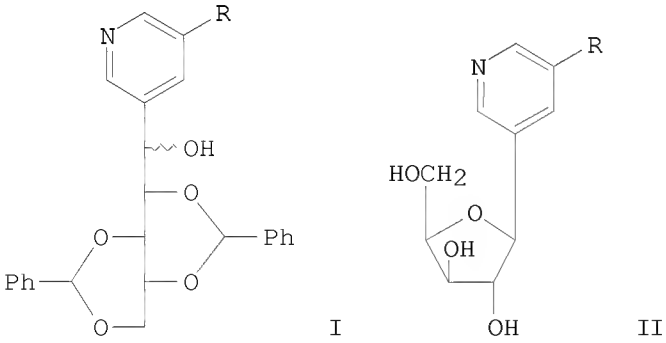
AB The title compds. [I; R1-R3 = (un)substituted acyl] (II; R = R4 = H) or their acid salts, useful as immunol. adjuvants having virucidal, antitumor, and antiinflammatory activities, etc.,were prepared by deprotection of their precursors (II; R, R4 = protective group). Thus, 3,7-anhydro-2,4-dideoxy-4-[3-(R)-hydroxytetradecanoylamido]-5,6-di-[3-(R)-hydroxytetradecanoyl]-α-D-glycero-D- ido-octonic acid was prepared by hydrogenation of 3,7-anhydro-4-[3-(R)-benzyloxytetradecanoylamido]-5,6-di-[3-(R)-benzyloxytetradecanoyl]-2,4-dideoxy-8-O-triphenylmethyl-α-D-glycero-D- ido-octonic acid benzyl ester (5-step preparation from 2-[3-(R)-benzyloxytetradecanoylamido]-2-deoxy-4,6-O-isopropylidene-α-D-glucose given) over Pd/C in aqueous THF, followed by stirring of the intermediate deprotected benzyl ester for 48 h with p-MeC6H4SO3H in CHCl3.

L3 ANSWER 38 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1992:192338 CAPLUS
DOCUMENT NUMBER: 116:192338
TITLE: Analysis of interferon-gamma resistant mutants that are possibly defective in their signal mechanism

AUTHOR(S): Feng, G. S.; Dai, W.; Gupta, S. L.; Werner-Felmayer, G.; Wachter, H.; Takikawa, O.; Taylor, M. W.
CORPORATE SOURCE: Dep. Biol., Indiana Univ., Bloomington, IN, 47405, USA
SOURCE: Molecular and General Genetics (1991), 230(1-2), 91-6
CODEN: MGGEAE; ISSN: 0026-8925
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Previous observations have indicated that mutants partially resistant to IFN-γ cytotoxicity were defective in the induction of indoleamine 2,3-dioxygenase, (IDO). Two mutants highly resistant to IFN-γ were isolated following a second round of mutagenesis. The resistance to IFN-γ was inversely correlated with the inducibility of IDO in these mutants. Moreover, several other IFN-γ responsive genes, including those encoding 2-5A synthetase, GTP cyclohydrolase, and HLA-DRα, were also differentially altered in their expression upon INF-γ treatment. IFN-γ receptor gene expression was not changed nor was the binding of the receptor to IFN-γ. Southern blot anal. failed to reveal any abnormality in the IDO gene structure in these mutants. These mutants may be defective in the IFN-γ signaling pathway and will be useful in further anal. of the biochem. mechanisms of IFN-γ activated gene expression in target cells.

L3 ANSWER 39 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1992:152268 CAPLUS
DOCUMENT NUMBER: 116:152268
TITLE: Synthesis and biological evaluation of some D-xylofuranosylpyridine C-nucleosides
AUTHOR(S): Verberckmoes, F.; Esmans, E. L.; Dommisse, R. A.; Lepoivre, J. A.; Alderweireldt, F. C.; Balzarini, J.; De Clercq, E.
CORPORATE SOURCE: Lab. Org. Chem., Univ. Antwerp, Antwerp, B-2020, Belg.
SOURCE: Nucleosides & Nucleotides (1991), 10(8), 1771-87
CODEN: NUNUD5; ISSN: 0732-8311
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 116:152268
GI



AB The addition reaction of either 3-bromo-5-lithiopyridine or 3-cyano-5-lithiopyridine to 2,4:3,5-di-O-benzylidene-aldehydo-D-xylose gave a D-gulo/D-ido mixture of resp. bromo- and cyano(dibenzylidenepentitolyl)pyridine I (R = Br, cyano). Mesylation of C-1' followed by reaction with CF3CO2H-H2O resulted in the formation of

the corresponding D-xylo-furanosylpyridine C-nucleosides, e.g., II. 3-Cyano-5-D-xylofuranosylpyridine II (R = cyano) was converted to 3-carbamoyl-5-D-xylofuranosylpyridines, e.g., II (R = CONH2), with Amberlite IRA 400 (OH-). The D-xylofuranosyl C-nucleosides were evaluated for their antiviral and cytostatic activity. No significant activity was found.

L3 ANSWER 40 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1992:104074 CAPLUS
DOCUMENT NUMBER: 116:104074
TITLE: The role of tryptophan and kynurenine transport in the catabolism of tryptophan through indoleamine 2,3-dioxygenase
AUTHOR(S): Knowles, R. G.; Clarkson, N. A.; Pogson, C. I.; Salter, M.; Duch, D. S.; Edelstein, M. P.
CORPORATE SOURCE: Wellcome Res. Lab., Beckenham/Kent, BR3 3BS, UK
SOURCE: Advances in Experimental Medicine and Biology (1991), 294(Kynurenine Serotonin Pathways), 161-6
CODEN: AEMBAP; ISSN: 0065-2598
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In this report studies were carried out on tryptophan metabolism and transport and on the intracellular concns. of tryptophan and kynurenine in cells in which indoleamine dioxygenase was induced in order to elucidate the role of the plasma membrane transport of tryptophan and kynurenine in the antitumor effects of IFNγ.

L3 ANSWER 41 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1992:34027 CAPLUS
DOCUMENT NUMBER: 116:34027
TITLE: Immunological effects of levamisole in vitro
AUTHOR(S): Schiller, Joan H.; Lindstrom, Mary; Witt, Patricia L.; Hank, Jacquelyn A.; Mahvi, David; Wagner, Randall J.; Sondel, Paul; Borden, Ernest C.
CORPORATE SOURCE: Dep. Hum. Oncol., William S. Middleton V. A. Hosp., Madison, WI, 53705, USA
SOURCE: Journal of Immunotherapy (1991-1992) (1991), 10(5), 297-306
CODEN: JOIME7; ISSN: 1053-8550
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Levamisole, an antihelminthic drug with immunol. properties, has antitumor activity when administered with 5-fluorouracil in patients with Duke's C colorectal carcinoma. The mechanism of this antitumor effect is unknown, but is postulated to be related to levamisole's immunomodulatory properties. To define further the immunomodulatory activities of levamisole, the authors examined the in vitro effects of levamisole on monocyte and lymphocyte cytotoxicity, activation, and proliferation; induction of cytokine-induced proteins; and expression of tumor -associated antigens. Expts. utilized peripheral blood mononuclear cells from normal donors incubated in the presence of increasing concns. of levamisole (0.1 to 100 μg/mL). Levamisole had no consistent effect on induction of 2',5'-oligoadenylate synthetase or indoleamine -2,3-dioxygenase activity, or production of tumor necrosis factor. Levamisole had no effect on monocyte cytotoxicity or expression of HLA-DR, HLA-DQ, HLA-DP, and the Fc receptor. Similarly, levamisole had no significant effect on NK or LAK cytotoxicity or the immunol. activation of T-lymphocytes, assessed by expression of CD3, CD4, CD8, CD16, CD25, and CD56. Proliferation of lymphocytes from normal donors, patients with benign polyps, and patients with malignancies, with or without IL-2 or irradiated LS174T cells, was not significantly increased overall. No

significant enhancement in the expression of three tumor-associated antigens (880364, NRCO-4, and ING-1) and the intercellular adhesion mol.-1 (ICAM-1) antigen on 4 human cancer cell lines was observed following in vitro exposure to levamisole. Thus, levamisole is not a potent modulator of the immune parameters examined, and the mechanism behind the unique clin. interaction between levamisole and 5-fluorouracil in colorectal carcinoma remains to be identified.

L3 ANSWER 42 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1991:551259 CAPLUS
DOCUMENT NUMBER: 115:151259
TITLE: Effects of melatonin on the cell cycle kinetics and "estrogen-rescue" of MCF-7 human breast cancer cells in culture
AUTHOR(S): Cos, Samuel; Blask, David E.; Lemus-Wilson, Athena; Hill, Anna B.
CORPORATE SOURCE: Coll. Med., Univ. Arizona, Tucson, AZ, 85724, USA
SOURCE: Journal of Pineal Research (1991), 10(1), 36-42
CODEN: JPRSE9; ISSN: 0742-3098
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Melatonin has been shown to have a direct inhibitory action on the proliferation of estrogen-responsive MCF-7 human breast cancer cells in culture. This inhibitory effect might be exerted on the G1 phase of the cell cycle, thus causing a transition delay into the S phase. In order to further verify this hypothesis the ability of estradiol to "rescue" MCF-7 cells from melatonin inhibition was tested and the potential of this indoleamine to block the ability of estradiol to rescue the cells from tamoxifen inhibition. Following five days of incubation, melatonin (10-9M) increased the fraction of cells in G1 of the cell cycle while simultaneously causing a 50% reduction in the proportion of cells in S phase. The antiproliferative effect of melatonin (10-5M) was prevented by the simultaneous treatment of the cells with estradiol (10-8M) in clonogenic soft agar culture, or reversed by the addition of estradiol to cells previously incubated with and inhibited by melatonin (10-9M) in monolayer culture. Addnl., melatonin blocked the estrogen-rescue of tamoxifen-inhibited cells in both types of culture systems. These results support the hypothesis that the antiproliferative effect of melatonin, like tamoxifen, is cell cycle specific by causing a G1-S transition delay. These results also indicate an important interaction of melatonin with estrogen-mediated mechanisms of MCF-7 cell proliferation.

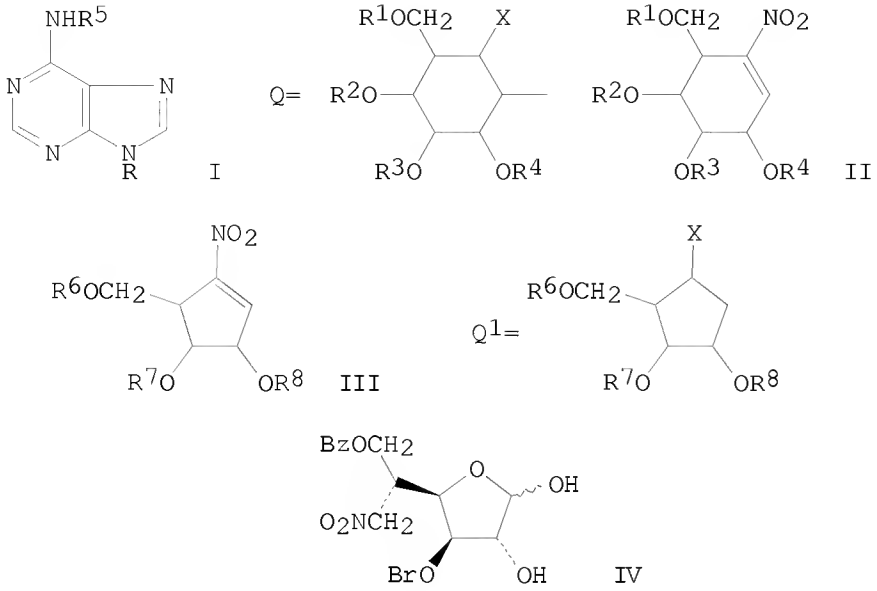
L3 ANSWER 43 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1990:550478 CAPLUS
DOCUMENT NUMBER: 113:150478
TITLE: IFN-γ is the inducer of indoleamine 2,3-dioxygenase in allografted tumor cells undergoing rejection
AUTHOR(S): Takikawa, Osamu; Habara-Ohkubo, Akemi; Yoshida, Ryotaro
CORPORATE SOURCE: Dep. Cell Biol., Osaka Biosci. Inst., Suita, 565, Japan
SOURCE: Journal of Immunology (1990), 145(4), 1246-50
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The depletion of an essential amino acid, tryptophan, caused by induction of indoleamine 2,3-dioxygenase (IDO), has been shown to be a mechanism involving self-defense against inhaled microorganisms

and tumor growth. Recently, it was reported that the IDO is (.apprx.50-fold) induced in allografted tumor (3-methylcholanthrene-induced ascites type tumor cells) cells undergoing rejection, and that the enzyme is induced by factor(s) released through the interaction of allografted tumor cells with infiltrating leukocytes. The culture supernatant of infiltrating leukocytes, which were harvested on day 7 after tumor transplantation, induced the highest IDO activity in the tumor cells. The inducer activity was completely neutralized by the addition of antibody to IFN-γ but not by antibody to IFN-α/β. Approx. 6 U/mL of IFN-γ was detected by an ELISA assay in the 12-h culture supernatant with 2 + 106 leukocytes/mL, and rIFN-γ at 6 U/mL induced IDO in 3-methylcholanthrene-induced ascites type tumor cells to the same extent as IFN-γ in the culture supernatant. Moreover, i.p. administration of antibody to IFN-γ almost completely inhibited the induction of IDO in the allografted tumor cells. Thus, the factor responsible for IDO induction in the allografted tumor cells is IFN-γ.

L3 ANSWER 44 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1990:459786 CAPLUS
DOCUMENT NUMBER: 113:59786
TITLE: Preparation of carbocyclic adenine nucleoside analogs as virucides and antitumor agents
INVENTOR(S): Kitagawa, Isao
PATENT ASSIGNEE(S): Taisho Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 02017190	A	19900122	JP 1988-166523	19880704 <--

PRIORITY APPLN. INFO.: JP 1988-166523 19880704
OTHER SOURCE(S): MARPAT 113:59786
GI



AB The title compds. (I; R = Q, Q1; X = H; R1 - R4, R6 - R8 = H, protecting group; R5 = H, protecting group), having strong antitumor and antiviral activity (no data), are prepared in good yields by addition reaction of nitrohexene and nitropentene derivs. II and III (R1 - R4, R6 - R8 = protecting group) with N-protected adenines and denitration of the resulting I (R = Q, Q1; X = NO2; R1 - R8 = protecting group). Thus, treatment of a dehydrofuranose (IV; Bn = CH2Ph) with KF and 18-crown-6 ether in DMF at 23° for 3 h gave, after acetylation, pseudo-D-gluco-II (R1 = Bz, R2 = R4 = Ac, R3 = Bn) which was stirred 1 h at 0° with I (R = H, R5 = Bz) in DMF in the presence of KF and 18-crown-6 to give pseudo-D-gluco-I (R = Q, = NO2, R1 = R5 = Bz, R2 = R4 = Ac, R3 = Bn). Denitration of the latter with Bn3BH and azobisisobutyronitrile in benzene at 80° for 3 h gave pseudo-D-gluco-I (R = Q, X = H, R1 = R5 = Bz, R2 = R4 = Ac, R3 = Bn) which was saponified with 1% NaOH/MeOH and then debenzylated with Na in NH3(l)/THF at -78° to give 9-pseudo-β-D-glucopyranosyladenine, i.e. pseudo-D-gluco-I (R = Q, X = R1 = R5 = H). Also prepared were pseudo-L-ido-I (R = X, X = R1 - R5 = H) and pseudo-L-xylo-I (R = Q1, X = R1 - R5 = H).

L3 ANSWER 45 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1990:53442 CAPLUS
DOCUMENT NUMBER: 112:53442
TITLE: Synergistic effects of phorbol ester and INF-γ on the induction of indoleamine 2,3-dioxygenase in THP-1 monocytic leukemia cells
AUTHOR(S): Edelstein, Mark P.; Ozaki, Yoshisuke; Duch, David S.
CORPORATE SOURCE: Dep. Med. Biochem., Wellcome Res. Lab., Research Triangle Park, NC, 27709, USA
SOURCE: Journal of Immunology (1989), 143(9), 2969-73
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Indoleamine 2,3-dioxygenase (IDO) is a flavin-dependent enzyme which uses superoxide anion as a cosubstrate to catalyze the decyclization of the pyrrole ring of L-tryptophan to form

formylkynurenine. This enzyme is induced in some tumor cells after treatment with IFN-γ. The mechanism of induction of IDO in tumor cells by IFN-γ was studied in THP-1 human monocytic leukemia cells. Before the addition of IFN-γ no IDO could be detected in these cells. Treatment of THP-1 cells with IFN-γ produced an induction of IDO, with peak activity occurring 72 to 96 h after addition of IFN-γ. Because phorbol esters are known to induce many enzymes in cells, most likely through the activation of protein kinase C, the effects of PMA on the induction of IDO were determined PMA potentiated the IFN-γ-induced elevation of IDO, but by itself, was unable to induce enzyme activity. Maximum induction of IDO in the presence of PMA and IFN-γ was obtained by preexposure of the cells to PMA for 78 h before the addition of IFN-γ. Maximum induction of IDO after the addition of IFN-γ occurred 24-48 h after addition of the cytokine to the culture medium. However, the induction of IDO does not appear to be potentiated through the activation of protein kinase C, because the addition of the protein kinase C inhibitor H-7 had no effect on the induction of IDO when the cells were exposed to PMA and IFN-γ. Moreover, diacylglycerol was unable to replace PMA in these studies. Studies with cAMP and cGMP analogs suggest a role for these compds. in the regulation of IDO expression.

L3 ANSWER 46 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1990:34224 CAPLUS
DOCUMENT NUMBER: 112:34224
TITLE: The effects of human interferons and retinoic acid on human neuroblastoma cells. Morphological differentiation and induction of 2',5'-oligoadenylate synthetase, protein kinase and indoleamine dioxygenase
AUTHOR(S): Hiratani, Hajime
CORPORATE SOURCE: Dep. Microbiol., Kyoto Prefect. Univ. Med., Kyoto, Japan
SOURCE: Kyoto-furitsu Ika Daigaku Zasshi (1989), 98(9), 961-80
CODEN: KFIZAO; ISSN: 0023-6012
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB Human interferon-γ (HuIFN-γ), dibutyryl cAMP, and bromodeoxyuridine were screened for the ability to induce morphol. differentiation of a human neuroblastoma (NB) GOTO cell line, in vitro. In particular, HuIFN-γ induced both the extension of complicatedly branched neurites and the formation of giant cells in NB cells. Although with the treatment of retinoic acid (RA) the morphol. differentiation did not occur, with the combination of HuIFN-γ and RA, intensified effects were shown. The 2'-5'-oligoadenylate synthetase (2-5AS), which is dependent on double stranded RNA (ds-RNA), was induced in NB cells by HuIFN-γ treatment. However, its activity in the HuIFN-γ-treated NB cells was far less than that in HuIFN-α- or HuIFN-β-treated NB cells. HuIFN-γ induced also ds-RNA-dependent protein kinase (PK) in NB cells. However, its activity was far less than that in HuIFN-α- or HuIFN-β-treated cells, as well as 2-5AS. RA intensified the effects of HuIFN-γ in terms of morphol. differentiation, but it did not increase the activity of 2-5AS and PK. Induction of indoleamine dioxygenase (IDO) activity was observed specifically in HuIFN-γ-treated NB cells. Since tryptophan was degraded to N-formyl kynurenine by the induction of IDO, the degraded tryptophan was complemented by the addnl. tryptophan to the culture medium. However, the induction of morphol. differentiation by HuIFN-γ treatment could not be inhibited. N-Formyl kynurenine or kynurenine, which are the catabolites of

tryptophan, did not induce the morphol. differentiation on NB cells. Thus, the induction of morphol. differentiation by HuIFN-γ is not correlated to the induction of the enzymic activities such as 2-5AS, PK, and IDO.

L3 ANSWER 47 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1989:495020 CAPLUS
DOCUMENT NUMBER: 111:95020
TITLE: Interferons and indoleamine 2,3-dioxygenase: role in antimicrobial and antitumor effects
AUTHOR(S): Carlin, J. M.; Ozaki, Y.; Byrne, G. I.; Brown, R. R.; Borden, E. C.
CORPORATE SOURCE: Med. Sch., Univ. Wisconsin, Madison, WI, 53706, USA
SOURCE: Experientia (1989), 45(6), 535-41
CODEN: EXPEAM; ISSN: 0014-4754
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 71 refs. Indoleamine 2,3-dioxygenase (IDO) is an interferon (IFN)-induced protein that initiates the metabolism of tryptophan along the kynurenine pathway. Although IDO can be induced by IFN-γ in many cell types, only mononuclear phagocytes have been shown to be induced to decyclize tryptophan by all three IFN classes. Since tryptophan is an essential amino acid necessary for a variety of metabolic processes, depletion of available tryptophan may be an important mechanism for control of rapidly-dividing microbial pathogens and tumors. The effects of IFN-induced IDO on prokaryotic and eukaryotic pathogens, as well as on a variety of tumor cell lines, are described.

L3 ANSWER 48 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1989:110482 CAPLUS
DOCUMENT NUMBER: 110:110482
TITLE: Superoxygenase
AUTHOR(S): Yoshida, Ryotaro
CORPORATE SOURCE: Dep. Cell Biol., Osaka Biosci. Inst., Suita, Japan
SOURCE: Tanpakushitsu Kakusan Koso (1988), 33(16), 3048-53
CODEN: TAKKAJ; ISSN: 0039-9450
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review with 24 refs., of the enzymic characterization of indoleamine oxygenase, with discussions of its mechanism of induction and its relation to antitumor activity.

L3 ANSWER 49 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1988:129837 CAPLUS
DOCUMENT NUMBER: 108:129837
TITLE: Induction of indoleamine 2,3-dioxygenase: a mechanism of the antitumor activity of interferon γ
AUTHOR(S): Ozaki, Yoshisuke; Edelstein, Mark P.; Duch, David S.
CORPORATE SOURCE: Dep. Med. Biochem., Wellcome Res. Lab., Research Triangle Park, NC, 27709, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1988), 85(4), 1242-6
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The antiproliferative effects of interferon α (IFN-α) and interferon γ (IFN-γ) were found to be cell-dependent. Among the human cell lines examined, IFN-γ had a greater antiproliferative

effect against cell lines that exhibited induction of indoleamine 2,3-dioxygenase, such as the KB oral carcinoma or WiDr colon adenocarcinoma, than against those that lacked the enzyme activity, such as the SW480 colon adenocarcinoma or NCI-H128 small-cell lung carcinoma. Induction of this dioxygenase showed a clear temporal relationship with increased metabolism of L-tryptophan and the depletion of this amino acid in the culture medium. While 70-80% of D-tryptophan remained in the medium of IFN-α- or vehicle-treated cells, virtually all of this amino acid was depleted in the medium of the IFN-γ-treated group following 2-3 days of culture. Supplementing the growth medium with addnl. L-tryptophan reversed the antiproliferative effect of IFN-γ against KB cells in a dose- and time-dependent manner. The antiproliferative effects of IFN-α and IFN-γ on SW480 and NCI-H128 cells, which are independent of the dioxygenase activity, and the inability of added L-tryptophan to reverse the effects of IFN-γ in WiDr cells suggest multiple mechanisms of action of the IFNs. The antiproliferative effect of IFN-γ through induction of indoleamine 2,3-dioxygenase, with a consequent L-tryptophan deprivation, is an effective means of regulating cell growth.

L3 ANSWER 50 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1988:110590 CAPLUS
DOCUMENT NUMBER: 108:110590
TITLE: Mechanism of interferon-γ action. Characterization of indoleamine 2,3-dioxygenase in cultured human cells induced by interferon-γ and evaluation of the enzyme-mediated tryptophan degradation in its anticellular activity
AUTHOR(S): Takikawa, Osamu; Kuroiwa, Takekiyo; Yamazaki, Fumio; Kido, Ryo
CORPORATE SOURCE: Dep. Biochem., Wakayama Med. Coll., Wakayama, 640, Japan
SOURCE: Journal of Biological Chemistry (1988), 263(4), 2041-8
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Induction by interferon-γ of indoleamine 2,3-dioxygenase (a tryptophan degradation enzyme) was examined in human cell lines. The enzyme induction was demonstrated in 7 of the 11 cell lines. The induced enzyme in each of the 7 cell lines was identical to the enzyme purified from human placenta, as evidenced by immunoblot anal. with a monoclonal antibody specific to the placental one. The extent of the induction varied largely with the cell line; a relatively high induction was observed with HEL (lung fibroblasts), NY (osteosarcoma), and A-431 (epidermoid carcinoma). The enzyme induction was dependent on the concentration of interferon-γ and occurred 12-18 h after addition of interferon-γ to the cultures. Interferon-α or -β was completely ineffective. Interferon-γ inhibited the growth of the 7 cell lines observed with the enzyme induction, and this growth inhibition was accompanied with a complete deletion of tryptophan (<1 μM) in the culture medium by the induction of the enzyme. For 2 of these cell lines, the inhibition was partially reversed by an addition of exogenous tryptophan to the medium. Thus, the growth inhibition by interferon-γ can in part be explained by the tryptophan depletion in the medium caused by the enzyme induction.

L3 ANSWER 51 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1987:509832 CAPLUS
DOCUMENT NUMBER: 107:109832
TITLE: Growth-inhibiting effect of crude pineal extracts on

human melanoma cells in vitro is different from that of known synthetic pineal substances

AUTHOR(S): Bartsch, Hella; Bartsch, C.; Noteborn, H. P. J. M.; Flehmig, B.; Ebels, I.; Salemink, C. A.

CORPORATE SOURCE: Inst. Hyg., Univ. Tuebingen, Tuebingen, D-7400, Fed. Rep. Ger.

SOURCE: Journal of Neural Transmission (1972-1989) (1987), 69(3-4), 299-311
CODEN: JNTMAH; ISSN: 0300-9564

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The effects of a number of synthetic indoleamines, pteridines, β-carbolines, arginine vasotocin, and crude exts. from rat and ovine pineal glands on human melanoma cells were studied in vitro. The identified pineal substances as well as some of their analogs showed an inhibitory effect only at nonphysiol. high concns. However, crude pineal exts. were more active than the synthetic pineal substances tested. They contain a compound which may have a tumor-inhibiting potency comparable to that of methotrexate but with a different mechanism of action.

L3 ANSWER 52 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1986:218611 CAPLUS

DOCUMENT NUMBER: 104:218611

ORIGINAL REFERENCE NO.: 104:34477a,34480a

TITLE: Efficient breakage of DNA apurinic sites by the indoleamine related 9-amino-ellipticine

AUTHOR(S): Malvy, Claude; Prevost, Philippe; Gansser, Charles; Viel, Claude; Paoletti, Claude

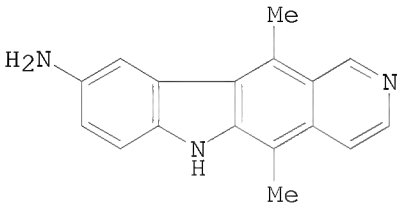
CORPORATE SOURCE: INSERM, Villejuif, 94800, Fr.

SOURCE: Chemico-Biological Interactions (1986), 57(1), 41-53
CODEN: CBINA8; ISSN: 0009-2797

DOCUMENT TYPE: Journal

LANGUAGE: English

GI

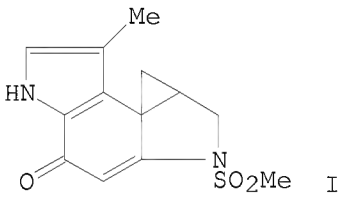


I

AB The aromatic amine, 9-NH2-ellipticine (I) [54779-53-2], is a synthetic DNA intercalating derivative of the antitumor agent ellipticine, which breaks circular DNA containing apurinic sites. This breakage is inhibited when the apurinic (AP) sites are reduced. The concentration of 9-NH2-ellipticine required to get a significant effect (0.1 μM) is the lowest known among chemical which induce the same breakage reaction. Comparison with the action of structurally related amines shows that the amino-indole structure is specific for AP sites. The ability of ellipticine derivs. to induce breakage in DNA containing apurinic sites is related to the nucleophile substituent in position 9. Two ellipticine derivs. with known antitumor activity, BD 40 [65222-35-7] and 9-OH-ellipticine [51131-85-2], were able to break purified DNA at apurinic sites.

L3 ANSWER 53 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1984:421392 CAPLUS
DOCUMENT NUMBER: 101:21392
ORIGINAL REFERENCE NO.: 101:3374h,3375a
TITLE: Role of indoleamine 2,3-dioxygenase in the defense mechanism against tumor growth
AUTHOR(S): Yoshida, Ryotaro; Takikawa, Osamu; Yasui, Hiroaki; Hayaishi, Osamu
CORPORATE SOURCE: Fac. Med., Kyoto Univ., Kyoto, 606, Japan
SOURCE: Prog. Tryptophan Serotonin Res., Proc. - Meet. Int. Study Group Tryptophan Res. ISTRY, 4th (1984), Meeting Date 1983, 513-16. Editor(s): Schlossberger, Hans Georg. de Gruyter: Berlin, Fed. Rep. Ger.
CODEN: 51OLA5
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Indoleamine 2,3-dioxygenase (IDO) was induced in tumor cells injected i.p. into allogenic strains of mice but not in tumor cells injected into syngeneic animals. Studies suggested that a decrease in the intracellular concentration of tryptophan, the substrate for IDO, caused tumor growth inhibition.

L3 ANSWER 54 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1981:532714 CAPLUS
DOCUMENT NUMBER: 95:132714
ORIGINAL REFERENCE NO.: 95:22223a,22226a
TITLE: Synthesis of the left-hand segment of the antitumor agent CC-1065
AUTHOR(S): Wierenga, Wendell
CORPORATE SOURCE: Upjohn Co., Kalamazoo, MI, 49001, USA
SOURCE: Journal of the American Chemical Society (1981), 103(18), 5621-3
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB A new, highly potent antitumor agent has recently been shown to be a trimer of pyrroloindoles, two of which are the same and have been prepared by Komoto et al. (1979). The unique segment, cyclopropylpyrroloindole I, has been prepared to isolate its biol. activity. Thus, 4-chloro-3-nitroanisole is converted to the indoline portion through a reductive cyclization. This is regiospecifically converted to the aminoindoline on which the methylindolic portion is elaborated via the Gassman indole chemical Ultimate intramol. para alkylation gave I.

L3 ANSWER 55 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1978:526647 CAPLUS
DOCUMENT NUMBER: 89:126647
ORIGINAL REFERENCE NO.: 89:19571a,19574a
TITLE: Uptake of biogenic amines by glial cells in culture.

I. A neuronal-like transport system for serotonin

AUTHOR(S): Suddith, R. L.; Hutchison, H. T.; Haber, B.

CORPORATE SOURCE: Mar. Biomed. Inst., Univ. Texas Med. Branch, Galveston, TX, USA

SOURCE: Life Sciences (1978), 22(24), 2179-87
CODEN: LIFSAK; ISSN: 0024-3205

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Rat C6 astrocytoma cells take up serotonin (5HT) via a high-affinity carrier-mediated system with Km = 1 μM, and a 2nd component of lower affinity. This high-affinity 5HT transport system was rapid, concentrative, and highly Na and temperature dependent. Chlorimipramine and Lilly 110140 preferentially blocked the glial 5HT but not norepinephrine uptake. This preferential inhibition had previously been shown for synaptosomes and brain slices. Norepinephrine, and to a lesser extent dopamine, blocked the glial 5HT uptake, suggesting a partial overlap between the catecholamine and indoleamine glial carrier systems. 5-Hydroxy-, but not 6-hydroxydopamine inhibited the high-affinity 5HT transport in glia. A variety of ring hydroxylated indoleamine analogs blocked this glial 5HT transport; of the compds. tested, 5,7-dihydroxytryptamine was the least effective inhibitor. Phenylethylamine and its O-methylated derivs. blocked synaptosomal and glial 5HT transport equally well. Thus, cultured C6 cells used as models of glia may possess a 5HT transport system which kinetically and pharmacol. resembles a neuronal 5HT transport system.

L3 ANSWER 56 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1978:105410 CAPLUS

DOCUMENT NUMBER: 88:105410

ORIGINAL REFERENCE NO.: 88:16545a,16548a

TITLE: 7-Substituted -7H-pyrrolo[3,2-f]quinazoline-1,3-diamines

INVENTOR(S): Ledig, Kurt Willi

PATENT ASSIGNEE(S): American Home Products Corp., USA

SOURCE: Ger. Offen., 112 pp.
CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

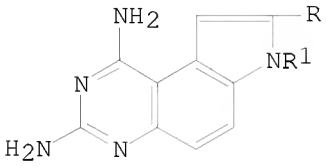
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
DE 2731039	A1	19780119	DE 1977-2731039	19770708	<--
ZA 7703939	A	19790228	ZA 1977-3939	19770629	<--
GB 1579678	A	19801119	GB 1977-27487	19770630	<--
AU 7726687	A	19790104	AU 1977-26687	19770701	<--
AU 507828	B2	19800228			
BE 856647	A1	19780109	BE 1977-179213	19770708	<--
DK 7703099	A	19780110	DK 1977-3099	19770708	<--
NL 7707658	A	19780111	NL 1977-7658	19770708	<--
FR 2357563	A1	19780203	FR 1977-21232	19770708	<--
FR 2357563	B1	19830311			
CH 634069	A5	19830114	CH 1977-8506	19770708	<--
IN 147488	A1	19800315	IN 1977-CA1610	19771115	<--
IN 147815	A1	19800705	IN 1979-CA874	19790823	<--
CH 635842	A5	19830429	CH 1982-2893	19820510	<--
CH 636616	A5	19830615	CH 1982-2894	19820510	<--

PRIORITY APPLN. INFO.:

US 1976-704001	A	19760709
US 1976-704002	A	19760709
GB 1976-53821	A	19761223
US 1977-784987	A	19770406

IE 1976-2853	A	19761231
US 1977-78987	A	19770406
CH 1977-8506	A	19770708
IN 1977-CA1610	A1	19771115

GI



I

AB Pyrroloquinazolinediamines I (R = H, Me, Ph, Cl; R1 = H, alkyl, cycloalkylmethyl, phenylalkyl, optionally substituted benzyl or Ph, naphthylmethyl, heterocyclylmethyl, heterocyclyl)(109 compds.) were prepared Thus, 5-aminoindole-HCl was condensed with HN(CN)2 to give I (R = R1 = H), which had a min. inhibitory concentration Staphylococcus aureus 31.3 mg/mL. Other I also showed antimalarial and antileukemic activity.

=>
=> d his

(FILE 'HOME' ENTERED AT 08:37:11 ON 22 JAN 2008)

FILE 'REGISTRY' ENTERED AT 08:37:32 ON 22 JAN 2008
E METHY-TH

FILE 'CAPLUS' ENTERED AT 08:37:59 ON 22 JAN 2008
L1 431 S (IDO OR 1MT OR INDOLEAMINE) AND INHIBITOR
L2 127 S L1 AND (CANCER OR TUMOR OR NEOPLASM)
L3 56 S L2 AND PY<=2003

=> logoff
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	197.20	197.87

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-44.80	-44.80

STN INTERNATIONAL LOGOFF AT 08:59:37 ON 22 JAN 2008

Connecting via Winsock to STN

Welcome to STN International! Enter x:X

LOGINID:ssptacrs1614

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	NOV 21	CAS patent coverage to include exemplified prophetic substances identified in English-, French-, German-, and Japanese-language basic patents from 2004-present
NEWS 3	NOV 26	MARPAT enhanced with FSORT command
NEWS 4	NOV 26	CHEMSAFE now available on STN Easy
NEWS 5	NOV 26	Two new SET commands increase convenience of STN searching
NEWS 6	DEC 01	ChemPort single article sales feature unavailable
NEWS 7	DEC 12	GBFULL now offers single source for full-text coverage of complete UK patent families
NEWS 8	DEC 17	Fifty-one pharmaceutical ingredients added to PS
NEWS 9	JAN 06	The retention policy for unread STNmail messages will change in 2009 for STN-Columbus and STN-Tokyo
NEWS 10	JAN 07	WPIDS, WPINDEX, and WPIX enhanced Japanese Patent Classification Data
NEWS 11	FEB 02	Simultaneous left and right truncation (SLART) added for CERAB, COMPUAB, ELCOM, and SOLIDSTATE
NEWS 12	FEB 02	GENBANK enhanced with SET PLURALS and SET SPELLING
NEWS 13	FEB 06	Patent sequence location (PSL) data added to USGENE
NEWS 14	FEB 10	COMPENDEX reloaded and enhanced
NEWS 15	FEB 11	WTEXTILES reloaded and enhanced
NEWS 16	FEB 19	New patent-examiner citations in 300,000 CA/CAplus patent records provide insights into related prior art
NEWS 17	FEB 19	Increase the precision of your patent queries -- use terms from the IPC Thesaurus, Version 2009.01
NEWS 18	FEB 23	Several formats for image display and print options discontinued in USPATFULL and USPAT2
NEWS 19	FEB 23	MEDLINE now offers more precise author group fields and 2009 MeSH terms
NEWS 20	FEB 23	TOXCENTER updates mirror those of MEDLINE - more precise author group fields and 2009 MeSH terms
NEWS 21	FEB 23	Three million new patent records blast AEROSPACE into STN patent clusters
NEWS 22	FEB 25	USGENE enhanced with patent family and legal status display data from INPADOCDB
NEWS 23	MAR 06	INPADOCDB and INPAFAMDB enhanced with new display formats
NEWS 24	MAR 11	EPFULL backfile enhanced with additional full-text applications and grants
NEWS 25	MAR 11	ESBIOBASE reloaded and enhanced

NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific

research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 10:05:06 ON 16 MAR 2009

=> file registry

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.22	0.22

FILE 'REGISTRY' ENTERED AT 10:05:16 ON 16 MAR 2009
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 13 MAR 2009 HIGHEST RN 1120564-02-4
DICTIONARY FILE UPDATES: 13 MAR 2009 HIGHEST RN 1120564-02-4

New CAS Information Use Policies, enter HELP USAGETERMS for details.

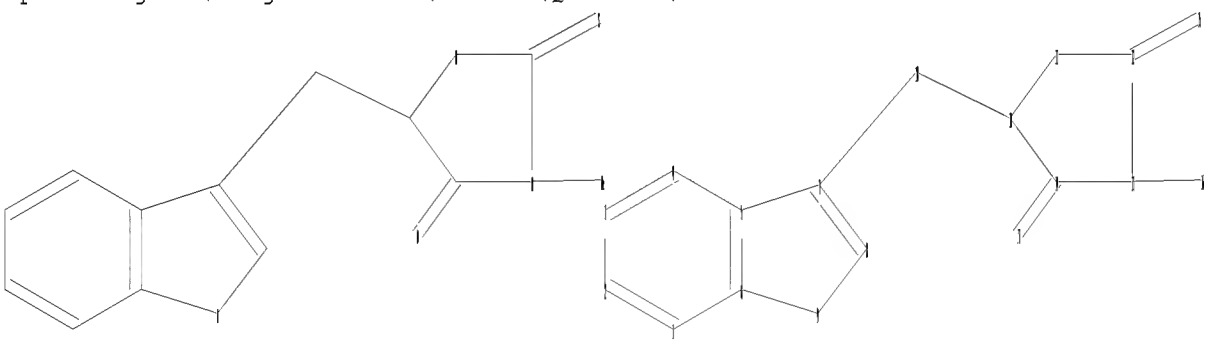
TSCA INFORMATION NOW CURRENT THROUGH January 9, 2009.

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\STNEXP\Queries\10551151.str



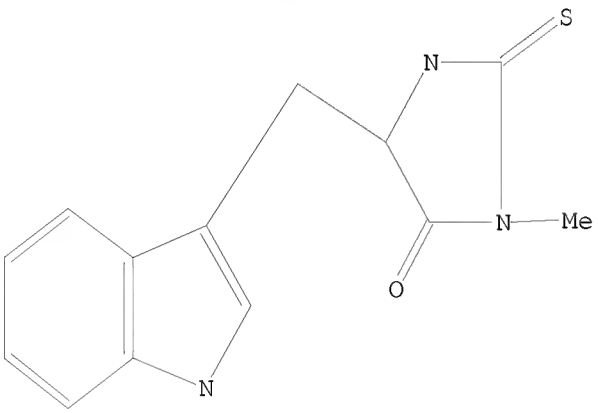
chain nodes :
15 16 17 18
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14
chain bonds :
7-18 10-18 12-15 13-16 14-17
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9 10-11 10-14 11-12 12-13 13-14

exact/norm bonds :
5-7 6-9 7-8 8-9 10-11 10-14 11-12 12-13 12-15 13-14 14-17
exact bonds :
7-18 10-18 13-16
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:CLASS 16:CLASS 17:CLASS 18:CLASS

L1   STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1   STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1 sss ful
FULL SEARCH INITIATED 10:05:40 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -   4401 TO ITERATE

100.0% PROCESSED   4401 ITERATIONS   25 ANSWERS
SEARCH TIME: 00.00.01

L2   25 SEA SSS FUL L1

=> s l1 fam ful
FULL SEARCH INITIATED 10:05:43 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -   105 TO ITERATE

100.0% PROCESSED   105 ITERATIONS   2 ANSWERS
SEARCH TIME: 00.00.01

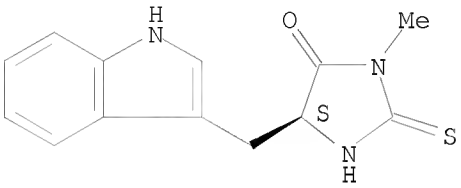
L3   2 SEA FAM FUL L1

=> d l3 1-2

L3   ANSWER 1 OF 2 REGISTRY COPYRIGHT 2009 ACS on STN
RN   28868-22-6 REGISTRY

ED Entered STN: 16 Nov 1984
CN 4-Imidazolidinone, 5-(1H-indol-3-ylmethyl)-3-methyl-2-thioxo-, (5S)- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Hydantoin, 5-(indol-3-ylmethyl)-3-methyl-2-thio-, L- (8CI)
FS STEREOSEARCH
MF C13 H13 N3 O S
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, USPAT2, USPATFULL
    (*File contains numerically searchable property data)

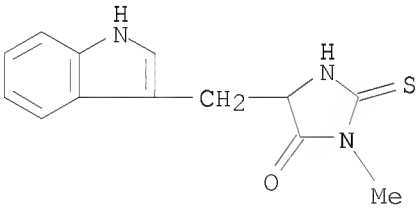
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2009 ACS on STN
RN 4311-88-0 REGISTRY
ED Entered STN: 16 Nov 1984
CN 4-Imidazolidinone, 5-(1H-indol-3-ylmethyl)-3-methyl-2-thioxo- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Hydantoin, 5-(indol-3-ylmethyl)-3-methyl-2-thio- (7CI, 8CI)
OTHER NAMES:
CN Nec 1
CN Necrostatin 1
DR 143443-40-7
MF C13 H13 N3 O S
LC STN Files: AGRICOLA, BEILSTEIN*, CA, CAPLUS, CASREACT, CHEMCATS, CSCHEM, PROUSDDR, TOXCENTER, USPAT2, USPATFULL
    (*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

31 REFERENCES IN FILE CA (1907 TO DATE)
31 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file caplus
COST IN U.S. DOLLARS SINCE FILE TOTAL

	ENTRY	SESSION
FULL ESTIMATED COST	262.83	263.05

FILE 'CAPLUS' ENTERED AT 10:06:09 ON 16 MAR 2009
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 16 Mar 2009 VOL 150 ISS 12
FILE LAST UPDATED: 15 Mar 2009 (20090315/ED)

Caplus now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2008.

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy.html

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l2
L4 34 L2

=> d l4 ibib abs 1-34

L4 ANSWER 1 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2008:1136027 CAPLUS
DOCUMENT NUMBER: 149:462087
TITLE: Structure-activity relationship study of a novel necroptosis inhibitor, necrostatin-7
AUTHOR(S): Zheng, Weihong; Degterev, Alexei; Hsu, Emily; Yuan, Junying; Yuan, Chengye
CORPORATE SOURCE: State Key Laboratory of Bio-Organic and Natural Product Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai, 200032, Peop. Rep. China
SOURCE: Bioorganic & Medicinal Chemistry Letters (2008), 18(18), 4932-4935
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Necroptosis is a regulated caspase-independent cell death mechanism characterized by morphol. features resembling non-regulated necrosis. Necrotatin-7 (Nec-7), a novel potent small-mol. inhibitor of necroptosis, is structurally distinct from previously described necrostatins (Nec-1, Nec-3, Nec-4 and Nec-5). Here, we describe a series of structural modifications and the structure-activity relationship (SAR) of the Nec-7 series for inhibiting necroptosis.
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2008:1021408 CAPLUS
DOCUMENT NUMBER: 150:206161
TITLE: Necrostatin-1 reduces histopathology and improves functional outcome after controlled cortical impact in mice
AUTHOR(S): You, Zerong; Savitz, Sean I.; Yang, Jinsheng; Degterev, Alexei; Yuan, Junying; Cuny, Gregory D.; Moskowitz, Michael A.; Whalen, Michael J.
CORPORATE SOURCE: Neuroscience Center, Massachusetts General Hospital, Harvard Medical School, Charlestown, MA, 02129, USA
SOURCE: Journal of Cerebral Blood Flow & Metabolism (2008), 28(9), 1564-1573
CODEN: JCBMDN; ISSN: 0271-678X
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Necroptosis is a newly identified type of programmed necrosis initiated by the activation of tumor necrosis factor alpha (TNFα)/Fas. Necrostatin-1 is a specific inhibitor of necroptosis that reduces ischemic tissue damage in exptl. stroke models. We previously reported decreased tissue damage and improved functional outcome after controlled cortical impact (CCI) in mice deficient in TNFα and Fas. Hence, we hypothesized that necrostatin-1 would reduce histopathol. and improve functional outcome after CCI in mice. Compared with vehicle-/inactive analog-treated controls, mice administered necrostatin-1 before CCI had decreased propidium iodide-pos. cells in the injured cortex and dentate gyrus (6 h), decreased brain tissue damage (days 14, 35), improved motor (days 1 to 7), and Morris water maze performance (days 8 to 14) after CCI. Improved spatial memory was observed even when drug was administered 15 mins after CCI. Necrostatin-1 treatment did not reduce caspase-3-pos. cells in the dentate gyrus or cortex, consistent with a known caspase-independent mechanism of necrostatin-1. However, necrostatin-1 reduced brain neutrophil influx and microglial activation at 48 h, suggesting a novel anti-inflammatory effect in traumatic brain injury (TBI). The data suggest that necroptosis plays a significant role in the pathogenesis of cell death and functional outcome after TBI and that necrostatin-1 may have therapeutic potential for patients with TBI. Journal of Cerebral Blood Flow & Metabolism (2008) 28, 1564-1573; doi:10.1038/jcbfm.2008.44; published online 21 May 2008.
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2008:530303 CAPLUS
DOCUMENT NUMBER: 149:69718
TITLE: A key in vivo antitumor mechanism of action of natural product-based brassinins is inhibition of indoleamine 2,3-dioxygenase
AUTHOR(S): Banerjee, T.; DuHadaway, J. B.; Gaspari, P.; Sutanto-Ward, E.; Munn, D. H.; Mellor, A. L.; Malachowski, W. P.; Prendergast, G. C.; Muller, A. J.
CORPORATE SOURCE: NewLink Genetics Corporation, Ames, IA, USA
SOURCE: Oncogene (2008), 27(20), 2851-2857
CODEN: ONCNES; ISSN: 0950-9232
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Agents that interfere with tumoral immune tolerance may be useful to prevent or treat cancer. Brassinin is a phytoalexin, a class of natural

products derived from plants that includes the widely known compound resveratrol. Brassinin has been demonstrated to have chemopreventive activity in preclin. models but the mechanisms underlying its anticancer properties are unknown. Here, we show that brassinin and a synthetic derivative 5-bromo-brassinin (5-Br-brassinin) are bioavailable inhibitors of indoleamine 2,3-dioxygenase (IDO), a pro-tolerogenic enzyme that drives immune escape in cancer. Like other known IDO inhibitors, both of these compds. combined with chemotherapy to elicit regression of autochthonous mammary gland tumors in MMTV-Neu mice. Furthermore, growth of highly aggressive melanoma isograft tumors was suppressed by single agent treatment with 5-Br-brassinin. This response to treatment was lost in athymic mice, indicating a requirement for active host T-cell immunity, and in IDO-null knockout mice, providing direct genetic evidence that IDO inhibition is essential to the antitumor mechanism of action of 5-Br-brassinin. The natural product brassinin thus provides the structural basis for a new class of compds. with in vivo anticancer activity that is mediated through the inhibition of IDO.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2008:480563 CAPLUS

DOCUMENT NUMBER: 149:44729

TITLE: Identification of RIP1 kinase as a specific cellular target of necrostatins

AUTHOR(S): Degterev, Alexei; Hitomi, Junichi; Germscheid, Megan; Ch'en, Irene L.; Korkina, Olga; Teng, Xin; Abbott, Derek; Cuny, Gregory D.; Yuan, Chengye; Wagner, Gerhard; Hedrick, Stephen M.; Gerber, Scott A.; Lugovskoy, Alexey; Yuan, Junying

CORPORATE SOURCE: Department of Biochemistry, School of Medicine, Tufts University, Boston, MA, 02111, USA

SOURCE: Nature Chemical Biology (2008), 4(5), 313-321
CODEN: NCBABT; ISSN: 1552-4450

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Necroptosis is a cellular mechanism of necrotic cell death induced by apoptotic stimuli in the form of death domain receptor engagement by their resp. ligands under conditions where apoptotic execution is prevented. Although it occurs under regulated conditions, necroptotic cell death is characterized by the same morphol. features as unregulated necrotic death. Here we report that necrostatin-1, a previously identified small-mol. inhibitor of necroptosis, is a selective allosteric inhibitor of the death domain receptor-associated adaptor kinase RIP1 in vitro. We show that RIP1 is the primary cellular target responsible for the antinecroptosis activity of necrostatin-1. In addition, we show that two other necrostatins, necrostatin-3 and necrostatin-5, also target the RIP1 kinase step in the necroptosis pathway, but through mechanisms distinct from that of necrostatin-1. Overall, our data establish necrostatins as the first-in-class inhibitors of RIP1 kinase, the key upstream kinase involved in the activation of necroptosis.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2008:421553 CAPLUS

DOCUMENT NUMBER: 149:298787

TITLE: Down-regulation of the indoleamine 2, 3-dioxygenase (IDO) transcription by tryptophan analogues

AUTHOR(S): Okamoto, Takeaki; Tone, Shigenobu; Kanoichi, Hiroaki; Ohyama, Fumio; Minatogawa, Yohsuke

CORPORATE SOURCE: Department of Biochemistry, Kawasaki Medical School, 577 Matsushima, Kurashiki, Okayama, 701-0192, Japan
SOURCE: International Congress Series (2007), 1304(Interdisciplinary Conference on Tryptophan and Related Substances: Chemistry, Biology, and Medicine, 2006), 352-356
CODEN: EXMDA4; ISSN: 0531-5131
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Indoleamine 2,3-dioxygenase (IDO; EC 1.13.11.42) is a rate-limiting enzyme involved in the catabolism of tryptophan, which is an essential amino acid. It is induced under pathol. conditions, such as the presence of viral infections or tumor cells. This enzyme is induced by IFN-γ in the mouse rectal carcinoma cell line CMT-93. It is known that both 1-methyl-L-tryptophan (1-MT) and methylthiohydantoin-DL-tryptophan (MTH-trp) are tryptophan analogs, and are authentic inhibitors of the enzymic activity of IDO. In this study, we examined the effects of both 1-MT and MTH-trp on the IFN-γ inducible IDO expression of CMT-93. As a result, the IFN-γ inducible IDO mRNA and the protein levels in CMT-93 were suppressed by 1-MT and MTH-trp, independently. Moreover, tryptophan (Trp), as a substrate of IDO, also suppressed IDO induction by IFN-γ at the transcriptional level. These results suggest that 1-MT and MTH-trp as inhibitors of IDO enzymic activity, and Trp suppress IDO induction by IFN-γ at the transcriptional level.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:1437629 CAPLUS
DOCUMENT NUMBER: 148:159932
TITLE: Necrostatin-1 protects against glutamate-induced glutathione depletion and caspase-independent cell death in HT-22 cells
AUTHOR(S): Xu, Xingshun; Chua, Chu C.; Kong, Jiming; Kostrzewa, Richard M.; Kumaraguru, Udayasankar; Hamdy, Ronald C.; Chua, Balvin H. L.
CORPORATE SOURCE: Department of Pharmacology, James H. Quillen College of Medicine, James H. Quillen Veterans Affairs Medical Center, East Tennessee State University, Johnson City, TN, USA
SOURCE: Journal of Neurochemistry (2007), 103(5), 2004-2014
CODEN: JONRA9; ISSN: 0022-3042
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Glutamate, a major excitatory neurotransmitter in the CNS, plays a critical role in neurol. disorders such as stroke and Parkinson's disease. Recent studies have suggested that glutamate excess can result in a form of cell death called glutamate-induced oxytosis. In this study, we explore the protective effects of necrostatin-1 (Nec-1), an inhibitor of necroptosis, on glutamate-induced oxytosis. We show that Nec-1 inhibits glutamate-induced oxytosis in HT-22 cells through a mechanism that involves an increase in cellular glutathione (GSH) levels as well as a reduction in reactive oxygen species production However, Nec-1 had no protective effect on free radical-induced cell death caused by hydrogen peroxide or menadione, which suggests that Nec-1 has no antioxidant effects. Interestingly, the protective effect of Nec-1 was still observed when cellular GSH was depleted by buthionine sulfoximine, a specific and irreversible inhibitor of glutamylcysteine synthetase. Our study further demonstrates that Nec-1 significantly blocks the nuclear translocation of

apoptosis-inducing factor (a marker of caspase-independent programmed cell death) and inhibits the integration of Bcl-2/adenovirus E1B 19 kDa-interacting protein 3 (a pro-death member of the Bcl-2 family) into the mitochondrial membrane. Taken together, these results demonstrate for the first time that Nec-1 prevents glutamate-induced oxytosis in HT-22 cells through GSH related as well as apoptosis-inducing factor and Bcl-2/adenovirus E1B 19 kDa-interacting protein 3-related pathways.
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:1397128 CAPLUS
DOCUMENT NUMBER: 148:553252
TITLE: The cardioprotective effect of necrostatin requires the cyclophilin-D component of the mitochondrial permeability transition pore
AUTHOR(S): Lim, S. Y.; Davidson, S. M.; Mocanu, M. M.; Yellon, D. M.; Smith, C. C. T.
CORPORATE SOURCE: The Hatter Cardiovascular Institute, University College London Hospital and Medical School, London, WC1E 6HX, UK
SOURCE: Cardiovascular Drugs and Therapy (2007), 21(6), 467-469
CODEN: CDTHET; ISSN: 0920-3206
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Necrostatin (Nec-1) protects against ischemia-reperfusion (IR) injury in both brain and heart. We have previously reported in this journal that necrostatin can delay opening of the mitochondrial permeability transition pore (MPTP) in isolated cardiomyocytes. The aim of the present study was to investigate in more detail the role played by the MPTP in necrostatin-mediated cardioprotection employing mice lacking a key component of the MPTP, namely cyclophilin-D. Anesthetized wild type (WT) and cyclophilin-D knockout (Cyp-D-/-) mice underwent an open-chest procedure involving 30 min of myocardial ischemia and 2 h of reperfusion, with subsequent infarct size assessed by triphenyltetrazolium staining. Nec-1, given at reperfusion, significantly limited infarct size in WT mice (17.7 ± 3% vs. 54.3 ± 3%, $P < 0.05$) but not in Cyp-D-/- mice (28.3 ± 7% vs. 30.8 ± 6%, $P > 0.05$). The data obtained in Cyp-D-/- mice provide further evidence that Nec-1 protects against myocardial IR injury by modulating MPTP opening at reperfusion.
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:1023773 CAPLUS
DOCUMENT NUMBER: 148:159407
TITLE: Necrostatin: A Potentially Novel Cardioprotective Agent?
AUTHOR(S): Smith, Christopher C. T.; Davidson, Sean M.; Lim, Shiang Y.; Simpkin, James C.; Hothersall, John S.; Yellon, Derek M.
CORPORATE SOURCE: Hatter Cardiovascular Institute, University College London Hospital and Medical School, London, WC1E 6HX, UK
SOURCE: Cardiovascular Drugs and Therapy (2007), 21(4), 227-233
CODEN: CDTHET; ISSN: 0920-3206
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Background: Necrostatin-1 (Nec-1), a small tryptophan-based mol., was recently reported to protect the cerebral cortex against ischemia-reperfusion (I/R) injury. We investigated the actions of Nec-1 and its so-called inactive analog, Nec-1i, in the setting of myocardial I/R injury. Materials and methods: The actions of Nec-1 and Nec-1i were examined in cultured C2C12 and H9c2 myocytes, cardiomyocytes isolated from male Sprague-Dawley rats, Langendorff isolated perfused C57Bl/6J mouse hearts and an in vivo open-chest C57Bl/6J mouse heart model. Results: Nec-1 at 30 μM and 100 μM (but not 100 μM Nec-1i) reduced peroxide-induced cell death in C2C12 cells from 51.2 ± 1.1% (control) to 26.3 ± 2.9% ($p < 0.01$ vs control) and 17.8 ± 0.9% ($p < 0.001$), resp. With H9c2 cells cell death was also reduced from 73.0 ± 0.4% (control) to 56.7 ± 0% (30 μM Nec-1, $p < 0.05$) and 45.4 ± 3.3% (100 μM Nec-1, $p < 0.01$). In the isolated perfused heart Nec-1 (30 μM) reduced infarct size (calculated as a percentage of the risk area) from 48.0 ± 2.0% (control) to 32.1 ± 5.4% ($p < 0.05$). Nec-1i (30 μM) also reduced infarct size (32.9 ± 5.1%, $p < 0.05$). In anesthetized C57Bl/6J mice Nec-1 (1.65 mg/kg), given i.p. to coincide with reperfusion following left anterior descending artery ligation (30 min), also reduced infarct size from 45.3 ± 5.1% (control) to 26.6 ± 4.0% ($p < 0.05$), while Nec-1i (1.74 mg/kg) was ineffective (37.8 ± 6.0%). Stimulus-induced opening of the mitochondrial permeability transition pore (MPTP) in rat cardiomyocytes, as reflected by the time until mitochondrial depolarization, was unaffected by Nec-1 or Nec-1i at 30 μM but increased at 100 μM i.e. 91% ($p < 0.05$ vs control) and 152% ($p < 0.001$) for Nec-1 and Nec-1i, resp. Conclusion: This is the first study to demonstrate that necrostatins inhibit myocardial cell death and reduce infarct size, possibly via a mechanism independent of the MPTP.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:830612 CAPLUS
DOCUMENT NUMBER: 148:282740
TITLE: Transcriptional regulation of indoleamine 2,3-dioxygenase (IDO) by tryptophan and its analogue
AUTHOR(S): Okamoto, Takeaki; Tone, Shigenobu; Kanouchi, Hiroaki; Miyawaki, Chie; Ono, Sayuri; Minatogawa, Yohsuke
CORPORATE SOURCE: Department of Biochemistry, Kawasaki Medical School, 577 Matsushima, Kurashiki, Okayama, 701-0192, Japan
SOURCE: Cytotechnology (2007), 54(2), 107-113
CODEN: CYTOER; ISSN: 0920-9069
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Indoleamine 2,3-dioxygenase (IDO; EC 1.13.11.42) is a rate-limiting enzyme involved in the catabolism of tryptophan, which is an essential amino acid. It is induced under pathol. conditions, such as the presence of viral infections or tumor cells. This enzyme is induced by IFN-γ in the mouse rectal carcinoma cell line CMT-93. It is known that both 1-methyl-l-tryptophan (1-MT) and methylthiohydantoin-dl-tryptophan (MTH-trp) are tryptophan analogs, and are authentic inhibitors of the enzymic activity of IDO. In this study, we examined the effects of both 1-MT and MTH-trp on the IFN-γ inducible IDO expression of CMT-93. As a result, the IFN-γ inducible IDO mRNA and the protein levels in CMT-93 were suppressed by 1-MT and MTH-trp, independently. Moreover, tryptophan (Trp), as a substrate of IDO, also suppressed IDO induction by IFN-γ at the transcriptional level. These results suggest that 1-MT and MTH-trp are as inhibitors of IDO enzymic activity, and Trp suppresses IDO induction by IFN-γ at the transcriptional level.
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

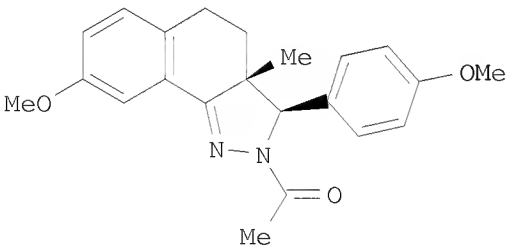
L4 ANSWER 10 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:730236 CAPLUS
DOCUMENT NUMBER: 147:143418
TITLE: Benzo[g]indazole, indole and tetralone compounds and their preparation, screening, and methods of treatment of diseases caused by TNFα or RIP1 protein
INVENTOR(S): Yuan, Junying; Degterev, Alexei; Hitomi, Junichi; Cuny, Gregory D.; Jagtap, Prakash
PATENT ASSIGNEE(S): President and Fellows of Harvard College, USA; The Brigham and Women's Hospital, Inc.
SOURCE: PCT Int. Appl., 263pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007075772	A2	20070705	WO 2006-US48583	20061220
WO 2007075772	A3	20090219		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
AU 2006331754	A1	20070705	AU 2006-331754	20061220
AU 2006331754	A2	20080814		
CA 2633500	A1	20070705	CA 2006-2633500	20061220
EP 1968583	A2	20080917	EP 2006-847822	20061220
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS				

PRIORITY APPLN. INFO.:

US 2005-751913P	P	20051220
US 2006-843304P	P	20060908
WO 2006-US48583	W	20061220

GI



I

AB The invention features compds., pharmaceutical compns., and methods for treating trauma, ischemia, stroke, degenerative diseases associated with cellular necrosis, and other conditions. Screening assays for identifying

compds. useful for treating these conditions are also described. Example compound I was prepared by a multistep procedure (procedure given). All the invention compds. were evaluated for their necrosis inhibitory activity and their structure-activity relationship.

L4 ANSWER 11 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:337477 CAPLUS
DOCUMENT NUMBER: 146:408284
TITLE: Application of alkannin to prepare medicine inducing cytoclasis programmed death
INVENTOR(S): Hu, Xun; Han, Weidong
PATENT ASSIGNEE(S): Zhejiang University, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 20pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1931152	A	20070321	CN 2006-10053627	20060927

PRIORITY APPLN. INFO.: CN 2006-10053627 20060927
AB The patent relates to application of alkannin((+)-5,8-dihydroxy-2-(1-hydroxy-4-methyl-3-pentenyl)-1,4-naphthoquinone) to prepare medicine(liquid prepns., granules, tablets, medicinal instant granules, gelatin pills, capsules, sustained-release preparation, dripping pills or injections) inducing cytoclasis programmed death, and the medicine is composed of alkannin and medical excipient or carrier. The alkannin can kill multidrug resistance tumor cells, and has low toxicity.

L4 ANSWER 12 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:157223 CAPLUS
DOCUMENT NUMBER: 147:65087
TITLE: Chemical genetic approaches to probing cell death
AUTHOR(S): Gangadhar, Nidhi M.; Stockwell, Brent R.
CORPORATE SOURCE: Department of Biological Sciences, 614 Fairchild Center, New York, NY, 10027, USA
SOURCE: Current Opinion in Chemical Biology (2007), 11(1), 83-87
CODEN: COCBF4; ISSN: 1367-5931
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Chemical genetics has arisen as a tool for the discovery of pathways and proteins in mammalian systems. This approach, comprising small-mol. screening combined with biochem. and genomic target identification methods, enables one to assess which proteins are involved in regulating a particular phenotype. Applied to cell death, this strategy can reveal novel targets and pathways regulating the demise of mammalian cells. Numerous diseases have been linked to the loss of regulation of cell death. Defining the mechanisms governing cell death in these diseases might lead to the discovery of therapeutic agents and targets and provide a richer understanding of the mortality of living systems. Recent advances include the discovery of novel small mols. regulating cell death pathways - necrostatin and erastin - as well as the elucidation of the mechanism of death induced in cancer cells by the cytotoxic agent Apratoxin A.
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:1084932 CAPLUS
DOCUMENT NUMBER: 144:22855
TITLE: Structure-activity relationship study of novel necroptosis inhibitors
AUTHOR(S): Teng, Xin; Degterev, Alexei; Jagtap, Prakash; Xing, Xuechao; Choi, Sungwoon; Denu, Regine; Yuan, Junying; Cuny, Gregory D.
CORPORATE SOURCE: Laboratory for Drug Discovery in Neurodegeneration, Harvard Center for Neurodegeneration and Repair, Brigham & Women's Hospital and Harvard Medical School, Cambridge, MA, 02139, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2005), 15(22), 5039-5044
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 144:22855
AB Necroptosis is a regulated caspase-independent cell death mechanism that results in morphol. features resembling necrosis. It can be induced in a FADD-deficient variant of human Jurkat T cells treated with TNF-α. 5-(1H-Indol-3-ylmethyl)-2-thiohydantoin derivs. and 5-(1H-indol-3-ylmethyl)hydantoin derivs. were found to be potent necroptosis inhibitors (called necrostatins). A SAR study revealed that several positions of the indole were intolerant of substitution, while small substituents at the 7-position resulted in increased inhibitory activity. The hydantoin ring was also quite sensitive to structural modifications. A representative member of this compound class demonstrated moderate pharmacokinetic characteristics and readily entered the central nervous system upon i.v. administration.
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:567526 CAPLUS
DOCUMENT NUMBER: 143:221812
TITLE: Chemical inhibitor of nonapoptotic cell death with therapeutic potential for ischemic brain injury
AUTHOR(S): Degterev, Alexei; Huang, Zhihong; Boyce, Michael; Li, Yaqiao; Jagtap, Prakash; Mizushima, Noboru; Cuny, Gregory D.; Mitchison, Timothy J.; Moskowitz, Michael A.; Yuan, Junying
CORPORATE SOURCE: Department of Cell Biology, Harvard Medical School, Boston, MA, 02115, USA
SOURCE: Nature Chemical Biology (2005), 1(2), 112-119
CODEN: NCBABT; ISSN: 1552-4450
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:221812
AB The mechanism of apoptosis has been extensively characterized over the past decade, but little is known about alternative forms of regulated cell death. Although stimulation of the Fas/TNFR receptor family triggers a canonical 'extrinsic' apoptosis pathway, the authors demonstrated that in the absence of intracellular apoptotic signaling it is capable of activating a common nonapoptotic death pathway, which the authors term necroptosis. The authors showed that necroptosis is characterized by necrotic cell death morphol. and activation of autophagy. The authors identified a specific and potent small-mol. inhibitor of necroptosis, necrostatin-1, which blocks a critical step in necroptosis. The authors demonstrated that necroptosis contributes to delayed mouse ischemic brain

injury in vivo through a mechanism distinct from that of apoptosis and offers a new therapeutic target for stroke with an extended window for neuroprotection. Our study identifies a previously undescribed basic cell-death pathway with potentially broad relevance to human pathologies.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

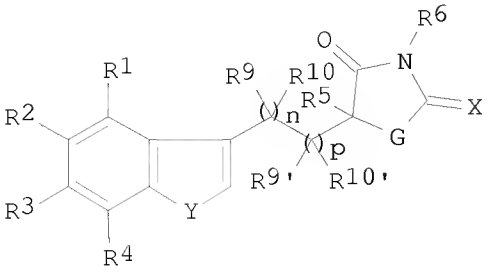
L4 ANSWER 15 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:474940 CAPLUS
DOCUMENT NUMBER: 143:26609
TITLE: Preparation of substituted indolyl-alkyl-imidazole/oxazole inhibitors of cellular necrosis
INVENTOR(S): Cuny, Gregory D.; Yuan, Junying; Jagtap, Prakash; Degterev, Alexei
PATENT ASSIGNEE(S): Brigham and Women's Hospital, Inc., USA; President and Fellows of Harvard College
SOURCE: U.S. Pat. Appl. Publ., 59 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

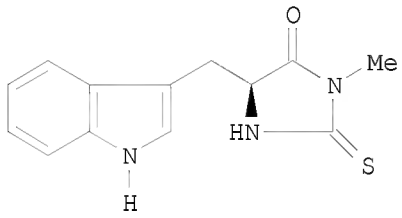
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20050119260	A1	20050602	US 2004-930690	20040830
US 7491743	B2	20090217		
AU 2004315596	A1	20050825	AU 2004-315596	20040830
CA 2536622	A1	20050825	CA 2004-2536622	20040830
WO 2005077344	A2	20050825	WO 2004-US28270	20040830
WO 2005077344	A3	20060316		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1663184	A2	20060607	EP 2004-821344	20040830
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
JP 2007504171	T	20070301	JP 2006-524953	20040830

PRIORITY APPLN. INFO.: US 2003-498882P P 20030829
WO 2004-US28270 W 20040830

OTHER SOURCE(S): CASREACT 143:26609; MARPAT 143:26609
GI



I



II

AB Title compds. I [X = O, S; Y = S, amino; G = O, amino; R1-3 = H, OH alkoxy, etc.; R4 = H, OH, alkoxy, halo, etc.; R5-6 = H, alkyl; R9-10' = H, F, Cl, Br, I, etc.; n, p = 0-5 with some provisos] are prepared For instance, L-tryptophan methylester is treated with methylisocyanate to give II. II in an assay of anti-necrotic activity using human Jurkat T cells, II has an EC50 = 6.0 μM for cell viability. I are useful in treating trauma, ischemia, stroke and degenerative diseases associated with cell death and are particularly useful for treating neurol. disorders.

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:369265 CAPLUS
DOCUMENT NUMBER: 142:423892
TITLE: Alanyl aminopeptidase inhibitors for functionally influencing different cells and treating immunological, inflammatory, neuronal, and other diseases
INVENTOR(S): Ansorge, Siegfried; Bank, Ute; Nordhoff, Karsten; Tager, Michael; Striggow, Frank
PATENT ASSIGNEE(S): Institut Fur Medizintechnologie Magdeburg GmbH IMTM, Germany; Keyneurotek AG
SOURCE: PCT Int. Appl., 332 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005037257	A2	20050428	WO 2004-EP11643	20041015
WO 2005037257	A3	20060914		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO,

NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ,
TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG

DE 10348023	A1	20050519	DE 2003-10348023	20031015
AU 2004281536	A1	20050428	AU 2004-281536	20041015
CA 2542723	A1	20050428	CA 2004-2542723	20041015
EP 1673075	A2	20060628	EP 2004-790485	20041015
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
CN 1897928	A	20070117	CN 2004-80036456	20041015
JP 2007508349	T	20070405	JP 2006-534706	20041015
US 20070037752	A1	20070215	US 2006-575882	20060915
PRIORITY APPLN. INFO.:			DE 2003-10348023 A	20031015
			WO 2004-EP11643 W	20041015

OTHER SOURCE(S): MARPAT 142:423892

AB The invention discloses substances which specifically inhibit peptidases splitting ala-p-nitroanilide for use in medicine. The invention further discloses the use of at least one such substance or at least one pharmaceutical or cosmetic composition containing such a substance for preventing and treating diseases, especially diseases with an overshooting immune response (autoimmune diseases, allergies, and transplant rejections), other chronic inflammatory diseases, neuronal diseases, brain damage, skin diseases (acne and psoriasis, among others), tumors, and special viral infections (including SARS).

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:927197 CAPLUS
DOCUMENT NUMBER: 141:388648
TITLE: Novel ido (indoleamine 2,3-dioxygenase) inhibitors and methods of use
INVENTOR(S): Prendergast, George C.; Muller, Alexander J.; Duhadaway, James B.; Malachowski, William
PATENT ASSIGNEE(S): Lankenau Institute for Medical Research, USA
SOURCE: PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004094409	A1	20041104	WO 2004-US5154	20040220
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2520586	A1	20041104	CA 2004-2520586	20040220
EP 1606285	A1	20051221	EP 2004-713430	20040220

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

CN 1795187	A	20060628	CN 2004-80008331		20040220
CN 1794986	A	20060628	CN 2004-80014321		20040220
JP 2006521377	T	20060921	JP 2006-508788		20040220
CN 101265254	A	20080917	CN 2008-10092243		20040220
CN 101265259	A	20080917	CN 2008-10092244		20040220
US 20070173524	A1	20070726	US 2006-550444		20060601
PRIORITY APPLN. INFO.:			US 2003-458162P	P	20030327
			US 2003-527449P	P	20031205
			CN 2004-80008331	A3	20040220
			WO 2004-US5154	W	20040220

OTHER SOURCE(S): MARPAT 141:388648

AB Novel inhibitors of indoleamine 2,3-dioxygenase (IDO) activity are provided. In yet another embodiment of the present invention, a combination treatment protocol comprising administration of an IDO inhibitor with a signal transduction inhibitor (STI) or chemotherapeutic agent is provided, which is effective for suppressing tumor growth. In still another embodiment of the present invention, a combination treatment protocol is provided for the treatment of a chronic viral infection, comprising the administration of an IDO inhibitor and a chemotherapeutic agent.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 18 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:927043 CAPLUS
DOCUMENT NUMBER: 141:388646
TITLE: Novel methods for the treatment of cancer and viral infections
INVENTOR(S): Prendergast, George C.; Muller, Alexander J.; Duhadaway, James B.; Malachowski, William
PATENT ASSIGNEE(S): Lankenau Institute for Medical Research, USA
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004093871	A1	20041104	WO 2004-US5155	20040220

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2520172	A1	20041104	CA 2004-2520172		20040220
EP 1613308	A1	20060111	EP 2004-713378		20040220

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

CN 1795187	A	20060628	CN 2004-80008331		20040220
CN 1794986	A	20060628	CN 2004-80014321		20040220
JP 2006521378	T	20060921	JP 2006-508789		20040220
CN 101265254	A	20080917	CN 2008-10092243		20040220
CN 101265259	A	20080917	CN 2008-10092244		20040220

US 20070099844 A1 20070503 US 2006-551151 20060518
PRIORITY APPLN. INFO.: US 2003-458162P P 20030327
US 2003-527449P P 20031205
CN 2004-80008331 A3 20040220
WO 2004-US5155 W 20040220

AB Compns. and methods for the treatment of malignancy and chronic viral infection are disclosed. A method is claimed for treating a cancer comprising administering at least one indoleamine 2,3-dioxygenase (IDO) inhibitor and at least one signal transduction inhibitor (STI). A method is claimed for treating a cancer comprising administering at least one immunomodulator, other than IDO inhibitor, and at least one cytotoxic chemotherapeutic agent or at least one STI. A method for treating a chronic viral infection in a patient is claimed comprising administering at least one IDO inhibitor and at least one chemotherapeutic agent. Pharmaceutical compns. containing compds. of the invention for treating cancer and viral infections are also claimed.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 19 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2001:300459 CAPLUS
DOCUMENT NUMBER: 134:320879
TITLE: Small molecule inhibitors of necrosis
INVENTOR(S): Yuan, Junying; Degterev, Alexei; Mitchison, Timothy
PATENT ASSIGNEE(S): President and Fellows of Harvard College, USA
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001028493	A2	20010426	WO 2000-US28475	20001013
WO 2001028493	A3	20010607		
W: CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6756394	B1	20040629	US 2000-688015	20001013
US 20050131044	A1	20050616	US 2004-880377	20040629
US 7253201	B2	20070807		

PRIORITY APPLN. INFO.: US 1999-159668P P 19991015
US 2000-174749P P 20000106
US 2000-688015 A1 20001013

OTHER SOURCE(S): MARPAT 134:320879

AB The invention features methods for decreasing necrosis. The invention also features methods for treating a subject with a condition in which necrosis occurs. The invention further features chemical compds. used to decrease necrosis.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 20 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1996:110170 CAPLUS
DOCUMENT NUMBER: 124:277362
ORIGINAL REFERENCE NO.: 124:50991a,50994a
TITLE: Reversed phase planar chromatography of enantiomeric compounds on microcrystalline triacetyl cellulose
AUTHOR(S): Lepri, Luciano
CORPORATE SOURCE: Dep. of Public Health, Epidemiology, and Environ. Analytical Chemistry, Univ. of Florence, Florence,

50121, Italy
SOURCE: Journal of Planar Chromatography--Modern TLC (1995), 8(6), 467-9
CODEN: JPCTE5; ISSN: 0933-4173
PUBLISHER: Research Institute for Medicinal Plants
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The aim of this work was to verify the resolving ability of microcryst. cellulose triacetate (MCTA) towards new structurally related racemates and to achieve further information about the contribution of the shape of the mol. and the polarity and the steric effects of the groups close to the asym. C, to chiral recognition. Retention and resolution data for enantiomeric compds. on MCTA plates with silica gel 60 GF254 as binder are given. A TLC of several racemates, pure optical isomers, and their mixts. on MCTA eluted with iso-PrOH-H2O, 60:40 (volume/volume) at 25° is presented: (±)-2-phenylbutyrophenone (a); R-(+)-1,1,2-triphenyl-1,2-ethanediol (b); S-(-)-1,1,2-triphenyl-1,2-ethanediol (c); mixture of (b) and (c); (2S)-(-)-3,3-dimethylglycidyl-4-nitrobenzoate (d); (2R)-(+)-3,3-dimethylglycidyl-4-nitrobenzoate (e); mixture of (d) and (e); (±)-carprofen; (S)-(-)-4-benzyl-2-oxazolidinone; (R)-(7)-4-benzyl-2-oxazolidinone; MTH-DL-Phe, MTH-DL-Tyr; MTH-DL-Pro; MTH-DL-Trp; MTH-DL-Leu; and PTH-DL-Trp. The role of the chemical characteristics of the solutes in chiral recognition was also addressed.

L4 ANSWER 21 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1992:551304 CAPLUS
DOCUMENT NUMBER: 117:151304
ORIGINAL REFERENCE NO.: 117:26229a,26232a
TITLE: Gas-chromatographic determination of methylthiohydantoin amino acid as N(O)-butyldimethylsilyl derivatives in amino acid sequencing with methylisothiocyanate
AUTHOR(S): Woo, Kang Lyung
CORPORATE SOURCE: Dep. Food Eng., Kyungnam Univ., Masan, 631-701, S. Korea
SOURCE: Han'guk Nonghwa Hakhoechi (1992), 35(2), 132-8
CODEN: JKACA7; ISSN: 0368-2897
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Derivatization of amino acids with new silylating reagent Me3CSiMe2NMeCOCF3 (I), instead of the usual N,O-bis(trimethylsilyl)acetamide (II) for the preparation of trimethylsilyl derivs., was used for effective determination of methylthiohydantoin amino acids from protein sequencing by GC on HP-1 capillary columns. Twenty one protein amino acids (except cystine) were identified using this method. Arginine, which is not detected by derivatization with II, was resolved with I. Multiple peaks were observed in derivatization of Pro, Ile, Gly, Tyr, and especially hydroxyproline with I. Calibration curves of the derivatized amino acid methylthiohydantions from 2.5 to 7.5 nmol showed good linearity, with Lys, His, and Arg showing linearity from 5.0 to 15.0 nmol. Correlation coeffs. and regression coeffs. of all calibration curves were highly significant ($\rho < 0.001$).

L4 ANSWER 22 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1989:87992 CAPLUS
DOCUMENT NUMBER: 110:87992
ORIGINAL REFERENCE NO.: 110:14369a,14372a
TITLE: Structural requirements for hydantoins and 2-thiohydantoins to induce lymphoproliferative popliteal lymph node reactions in the mouse

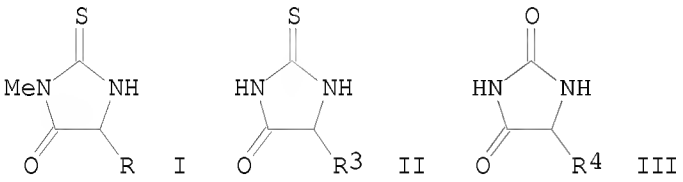
AUTHOR(S): Kammueller, Michael E.; Seinen, Willem
CORPORATE SOURCE: Fac. Vet. Sci., Univ. Utrecht, Utrecht, 3572 BP, Neth.
SOURCE: International Journal of Immunopharmacology (1988), 10(8), 997-1010
CODEN: IJIMDS; ISSN: 0192-0561
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The ability of a large number of hydantoins and 2-thiohydantoins to induce primary local lymphoproliferative popliteal lymph node (PLN) reactions was investigated, as judged by PLN weight enlargement, in an attempt to evaluate the discriminating potential of the PLN reaction to low-mol.-weight chems. and to establish structure-activity relationships. Among a series of 19 hydantoins and related compds. only 5,5-diphenylhydantoin (phenytoin), its major metabolite 5-(p-hydroxyphenyl)-5-phenylhydantoin, 5,5-diphenyl-2-thiohydantoin and N-(5-nitro-2-furfurylidene)-1-aminohydantoin (nitrofurantoin) elicited marked PLN reaction in C57BL/6J mice. In DBA/2 mice, PLN responses to the aforementioned compds. were considerably less or virtually absent. A number of hydantoin derivs. and related compds. with 1 Ph group and(or) other substituents at the 1, 3, or 5 position induced only slightly elevated or suppressed PLN responses in C57BL/6J mice. The influences of polar and lipophilic aliphatic and aromatic substituents at the 5 position were compared among a series of 22 3-methyl-2-thiohydantoin as well as 21 3-phenyl-2-thiohydantoin amino acid derivs. for their ability to elicit primary PLN reactions in C57BL/6J mice. Substitution with only 1 aromatic group at the 5 position seemed to be necessary to induce PLN enlargements by 2-thiohydantoins already substituted at the 3 position with a Me group or even more pronounced when substituted with a Ph group. p-Hydroxylation of 5-benzyl-3-phenyl-2-thiohydantoin diminished the PLN response. In contrast, p-hydroxylation of 1 of 2 Ph groups as in 5-(p-hydroxyphenyl)-5-phenylhydantoin had little effect on lymphoproliferative PLN reactions. The presence of an OH group in a nonarom. cyclic substituent as in hexahydro-6-hydroxy-2-methyl-3-thioxo-1H-pyrrolo[1,2-c]imidazol-1-one had no effect on the PLN reaction. Study of a series of aliphatic substituents in the 5 position of 2-thiohydantoins showed that the number of C atoms of the substituents as well as the position of side chains in the isomer, rather than the Me or Ph group in the 3 position of the 2-thiohydantoin mol., determined the strength of the PLN enlargement. Thus, the PLN weight increase assay appears to be able to discriminate between subtle chemical differences as studied with a large series of hydantoin and 2-thiohydantoin derivs. The PLN assay may therefore be useful as a preliminary short-term screening method for identification of (classes of) compds. able to induce lymphoproliferative reactions. However, the PLN assay did not identify all hydantoin derivs. and related compds. with documented lymphoproliferative side effects in humans. The possible significance of polymorphisms in drug metabolism and disposition, factors not accounted for by the local PLN reaction, is discussed.

L4 ANSWER 23 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1980:193679 CAPLUS
DOCUMENT NUMBER: 92:193679
ORIGINAL REFERENCE NO.: 92:31333a,31336a
TITLE: Methylthiohydantoin amino acids: chromatographic separation and comparison to phenylthiohydantoin amino acids
AUTHOR(S): Horn, Marcus J.; Hargrave, Paul A.; Wang, Janet K.
CORPORATE SOURCE: Sequemat Inc., Watertown, MA, 02172, USA
SOURCE: Journal of Chromatography (1979), 180(1), 111-18
CODEN: JOCRAM; ISSN: 0021-9673
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Most phenylthiohydantoin (PTH) amino acids and most methylthiohydantoin (MTH) amino acids could be separated from 1 another by thin-layer chromatog. (TLC) using the same sequential development technique with the same 2 solvents. Similarly, a single solvent system could be used in high-performance liquid chromatog. (HPLC) to sep. most PTH-amino acids and most MTH-amino acids. When both TLC and HPLC sepns. were performed on a sample, all MTH- and PTH-amino acids could be uniquely identified. Since many solid-phase protein sequencing techniques generate both MTH- and PTH-amino acids, these anal. systems simplify identification of the amino acid derivs. Although the chromatog. properties of MTH- and PTH-amino acids were similar, they were not identical.

L4 ANSWER 24 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1977:568372 CAPLUS
DOCUMENT NUMBER: 87:168372
ORIGINAL REFERENCE NO.: 87:26626h,26627a
TITLE: Proton nuclear magnetic resonance studies on methylthiohydantoins, thiohydantoins, and hydantoins of amino acids
AUTHOR(S): Suzuki, Tateo; Tomioka, Tetsuhisa; Tuzimura, Katura
CORPORATE SOURCE: Fac. Agric., Tohoku Univ., Sendai, Japan
SOURCE: Canadian Journal of Biochemistry (1977), 55(5), 521-7
CODEN: CJBIAE; ISSN: 0008-4018
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



AB The proton NMR of methylthiohydantoins I [R = R1 [R1 = H, Me, CHMe2, CH2CHMe2, CHMeEt, CH2Ph, CH2C6H4OH-p, CH2CH2SMe, CH2CO2H, (CH2)3NHC(:NH)NH2, indol-3-ylmethyl, imidazol-4-ylmethyl], R2 [R2 = CH2CONH2, CH2CH2CONH2), CH2SH, CH2CH2CO2H, (CH2)4NHCSMe]], thiohydantoins II [R3 = R1, R2, CH2SCH2CO2H, (CH2)4NHAc], and hydantoins III [R4 = R1, CH2OH, CH(OH)Me, CH2SO3H, CH2CH2CO2H, (CH2)4NHAc] were given for the identification of the parent amino acid. The N- and C-terminal residues of Leu-Gly-Gly were determined by an application of this proton NMR-hydantoin method.

L4 ANSWER 25 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1976:31395 CAPLUS
DOCUMENT NUMBER: 84:31395
ORIGINAL REFERENCE NO.: 84:5149a,5152a
TITLE: Folded conformation of substituted thiohydantoins of aromatic amino acids
AUTHOR(S): Siemion, I. Z.; Attia, I.; Nowak, K.
CORPORATE SOURCE: Inst. Chem., Univ. Joliot-Curie, Wroclaw, Pol.
SOURCE: Bulletin de l'Academie Polonaise des Sciences, Serie des Sciences Chimiques (1975), 23(7), 575-80
CODEN: BAPCAQ; ISSN: 0001-4095
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The NMR spectra of 3-phenyl(and methyl)-2-thiohydantoins of phenylalanine and tryptophan, and the 3-phenyl-2-thiohydantoins of alanine and glycine

show that the phenyl residues have magnetically nonequivalent protons, that protons in positions 1 and 5 of the thiohydantoin ring do not couple and the domination of the folded conformation.

L4 ANSWER 26 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1972:72760 CAPLUS
DOCUMENT NUMBER: 76:72760
ORIGINAL REFERENCE NO.: 76:11725a,11728a
TITLE: Metastable transitions in the mass spectra of methyl and phenylthiohydantoin derivatives of amino acids
AUTHOR(S): Sun, T.; Lovins, R. E.
CORPORATE SOURCE: Dep. Biochem., Univ. Georgia, Athens, GA, USA
SOURCE: Organic Mass Spectrometry (1972), 6(1), 39-45
CODEN: ORMSBG; ISSN: 0030-493X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The mass spectra of a number of methyl- (MTH) and phenylthiohydantoin (PTH) amino acid derivs. were obtained. The major metastable transitions occurring in the mass spectra of these derivs. were identified and measured. The major fragmentation pathways associated with the metastable transitions were outlined and discussed for each group of compds. Inspection of the metastable data has shown that there is at least one unique metastable transition occurring for each thiohydantoin derivative which may be used to uniquely identify that derivative in the presence of a mixture of thiohydantoin derivs. obtained from the Edman degradation of a peptide or protein. The use of metastable ions to uniquely identify thiohydantoin derivs. in mixts. has proven useful in the identification of the MTH and PTH derivatives of glycine whose mol. ions are not unique and for resolving such ambiguities as occur for example in the mixture of leucine and isoleucine.

L4 ANSWER 27 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1972:32002 CAPLUS
DOCUMENT NUMBER: 76:32002
ORIGINAL REFERENCE NO.: 76:5201a,5204a
TITLE: Quantitative protein sequencing using mass spectrometry. Use of low ionizing voltages in mass spectral analysis of methyl- and phenylthiohydantoin amino acid derivatives
AUTHOR(S): Sun, T.; Lovins, R. E.
CORPORATE SOURCE: Dep. Biochem., Univ. Georgia, Athens, GA, USA
SOURCE: Analytical Biochemistry (1972), 45(1), 176-91
CODEN: ANBCA2; ISSN: 0003-2697
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The mass spectra of 18 methylthiohydantoin and 13 phenylthiohydantoin amino acid derivs. have been recorded at electron energies of 11, 20, and 70 eV. The spectra of the majority of the derivs. were decreased in complexity, in some cases containing only the mol. ion. The mol. ion was generally the base peak of the low-voltage spectrum. The loss of sensitivity at lower ionizing voltages was measured for a number of compds. and the sensitivity as measured by ion abundance was maximum around 20 eV and decreased rapidly at lower energies. The use of low-energy electron impact ionization is compared to chemical ionization and the advantages and disadvantages discussed.

L4 ANSWER 28 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1971:60936 CAPLUS
DOCUMENT NUMBER: 74:60936
ORIGINAL REFERENCE NO.: 74:9793a,9796a
TITLE: Optical rotatory properties of

methylisothiocyanate-amino acid adducts
AUTHOR(S): Toniolo, Claudio
CORPORATE SOURCE: Ist. Chim. Org., Univ. Padova, Padua, Italy
SOURCE: Tetrahedron (1970), 26(23), 5479-88
CODEN: TETRAB; ISSN: 0040-4020
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Definite information concerning the optical configurations of amino acids in peptides has been obtained from an investigation of the CD of their adducts with methyl isothiocyanate.

L4 ANSWER 29 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1971:54160 CAPLUS
DOCUMENT NUMBER: 74:54160
ORIGINAL REFERENCE NO.: 74:8753a,8756a
TITLE: Gas chromatographic identification of the thiohydantoins of degradation products peptides and proteins
AUTHOR(S): Tschesche, Harald; Obermeier, Rainer; Kupfer, Sigrid
CORPORATE SOURCE: Lab. Org. Chem. Biochem., Tech. Univ. Muenchen, Munich, Fed. Rep. Ger.
SOURCE: Angewandte Chemie, International Edition in English (1970), 9(11), 893-4
CODEN: ACIEAY; ISSN: 0570-0833
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB Naturally occurring amino acids can be chromatographed as their 3-methyl-2-thiohydantoin derivs. (I). The acids, phenylalanine, asparagine, glutamine, tyrosine, and tryptophan, are chromatographed after treatment with MeNCS.

L4 ANSWER 30 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1970:488146 CAPLUS
DOCUMENT NUMBER: 73:88146
ORIGINAL REFERENCE NO.: 73:14417a,14420a
TITLE: Syntheses and gas chromatography of methylthiohydantoin-amino acids
AUTHOR(S): Okamoto, Hiroo; Okuyama, Tsuneo
CORPORATE SOURCE: Fac. Sci., Tokyo Metrop. Univ., Tokyo, Japan
SOURCE: Seikagaku (1969), 41(12), 850-9
CODEN: SEIKAQ; ISSN: 0037-1017
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB 3-Methyl-2-thiohydantoin derivs. of glycine, DL-alanine, L-valine, L-leucine, L-isoleucine, L-phenylalanine, DL-methionine, L-glutamate, DL-aspartate, L-glutamine, L-asparagine, L-threonine, L-serine, L-lysine, L-histidine, L-tyrosine, L-tryptophan, and L-proline were synthesized. Some of these derivs. of amino acids were separable by gas chromatography. Trimethylsilation of these derivs. enable the separation of all protein amino acids by gas chromatog. operated at 175-250°.

L4 ANSWER 31 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1970:133164 CAPLUS
DOCUMENT NUMBER: 72:133164
ORIGINAL REFERENCE NO.: 72:23851a,23854a
TITLE: Gas chromatography of methyl thiohydantoins of amino acids
AUTHOR(S): Attrill, James E.; Butts, William C.; Rainey, William T., Jr.; Holleman, James W.
CORPORATE SOURCE: Anal. Chem. Div., Oak Ridge Nat. Lab., Oak Ridge, TN, USA

SOURCE: Analytical Letters (1970), 3(2), 59-65
CODEN: ANALBP; ISSN: 0003-2719
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The methyl thiohydantoins of 22 amino acids commonly encountered in protein sequence work were prepared and their behavior on gas chromatog. investigated. Sixteen of these were separated from each other by 2 columns with different silicone stationary phases. The methyl thiohydantoins of aspartic acid, serine, arginine, carboxymethyl cysteine, and cysteic acid, which gave decomposition and a common peak in the above systems, gave unique peaks following silylation. The methyl thiohydantoin of cysteine was not successfully analyzed.

L4 ANSWER 32 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1969:430677 CAPLUS
DOCUMENT NUMBER: 71:30677
ORIGINAL REFERENCE NO.: 71:5677a
TITLE: Sequential degradation of proteins and peptides
AUTHOR(S): Richards, Frank F.; Barnes, William T.; Lovins, Robert E.; Salomone, Ramon; Waterfield, Michael D.
CORPORATE SOURCE: Sch. of Med., Yale Univ., New Haven, CT, USA
SOURCE: Nature (London, United Kingdom) (1969), 221(5187), 1241-4
CODEN: NATUAS; ISSN: 0028-0836
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A quant. protein degradation method using a volatile Edman reagent (MeNCS), an isotope dilution step for quantitation of the data, and an isotope ratio assay by conventional mass spectrometry is described. In this method, the peptide or protein is dissolved in 50% aqueous pyridine and reacted for 1 hr. at 60° with a 10 molar excess (based on available amino end groups) of MeNCS in the absence of O and light. In subsequent reactions with the 2nd NH2-terminal residue, only a 1.5 mole excess of MeNCS is required. To this aliquot is added a standardized solution containing a mixture of 20 Me thiohydantoin amino-acid derivs. which are enriched in 15N and for which the exact 14N/15N ratio is known for each derivative. Excess MeNCS is removed during 2 hrs. in vacuo at 6°. The residue is treated with CF3CO2H or CF3CF2CF2CO2H for 10 min., after which the excess acid is removed with N gas at 90°. This method promotes the formation of the cyclic thiohydantoin derivative from the N-terminal thiourea without detectable thiazolidone formation, and the product yields are >98%. Alternatively, it is possible to volatilize the thiohydantoin derivative using hot N and a sample trap to collect the volatized derivative Using these conditions, the method does not destroy the peptide. After removal of the excess acid, the residue is taken up in tetrahydrofuran, and a nonquant. aliquot containing 1-10 mg. thiohydantoins is transferred to a small capillary. The solvent is removed under vacuum, and the capillary is heated slowly in a mass spectrometer. This method permits partial separation, in order of volatility, making it easier to identify and determine the amts. of each Me thiohydantoin in the mixture The mass spectra are further simplified by using a low ionizing voltage (10 ev.) which produces spectra containing primarily the mol. ions and only a few of the more abundant fragment ions. Clearly identifiable mol. ions are observed for all derivs. except S-aminoethylcysteine (which may be identified by a fragment ion at m/e 150). Because of ambiguities, leucine and isoleucine are identified from fragment ions at m/e 143 and m/e 102, resp. To obtain quant. information from the mass spectra, the 14N/15N ratios in the mol. ion peaks of the derivs. present in the mixture are accurately determined from the recorded spectrum, and any contribution from other ions is subtracted. These ratios and the initial concentration of each 15N enriched derivative introduced

permit the determination of the exact amount of each Me thiohydantoin formed at each
N-terminal reaction. The derivs. of the common amino-acids are all sufficiently volatile to be used in this method.

L4 ANSWER 33 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1966:76023 CAPLUS
DOCUMENT NUMBER: 64:76023
ORIGINAL REFERENCE NO.: 64:14262e-f
TITLE: 3-Methyl-2-thiohydantoins of amino acids. IV. Separation of 3-methyl-2-thiohydantoins of amino acids by thin-layer chromatography on silica gel
AUTHOR(S): Stepanov, V. M.; Lapuk, Ya. I.
CORPORATE SOURCE: Inst. Chem. Natur. Prod., Moscow
SOURCE: Zhurnal Obshchei Khimii (1966), 36(1), 40-4
CODEN: ZOKHA4; ISSN: 0044-460X
DOCUMENT TYPE: Journal
LANGUAGE: Russian
AB cf. CA 62, 13137g; 63, 9934e. Methylthiohydantoins of natural amino acids, along with carboxymethyl-cysteine were separated by thin-layer chromatography on silica gel. The separation was readily followed after the carrier was treated with a luminophor which transforms uv light into visible light; the most satisfactory one was Zn silicate activated with Mn (Soviet preparation K-36), which gave ready location of the spots after illumination of the chromatographic plate with uv light. The solvents systems were composed of various proportions of CHCl3, EtOH, MeOH, HCO2H, and AcOH. For development of the spots p-Et2NC6H4NH2 proved to be more satisfactory than benzidine or tolidine.

L4 ANSWER 34 OF 34 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1965:403533 CAPLUS
DOCUMENT NUMBER: 63:3533
ORIGINAL REFERENCE NO.: 63:669e-g
TITLE: 3-Methyl-2-thiohydantoins of amino acids. II. Synthesis and properties of 3-methyl-2-thiohydantoins of heterocyclic and N-methylated amino acids, monoamidodicarboxylic acids, and their amides
AUTHOR(S): Krivtsov, V. F.; Stepanov, V. M.
CORPORATE SOURCE: Inst. Chem. Natural Products, Moscow
SOURCE: Zhurnal Obshchei Khimii (1965), 35(3), 556-9
CODEN: ZOKHA4; ISSN: 0044-460X
DOCUMENT TYPE: Journal
LANGUAGE: Russian
AB cf. CA 62, 13137g. DL-Proline-HCl in H2O treated with Me isothiocyanate at pH 9 (KOH) and 40° gave after 15 min. on acidification with HCl 26.5% DL-proline methylthiohydantoin, m. 51°. Similarly was prepared sarcosine methylthiohydantoin, m. 93°; and N-methylvaline methylthiohydantoin, m. 63°. Tryptophan treated as above in 40 hrs. gave 3-methyl-5-(3-indolylmethyl)-2-thiohydantoin, m. 151°. Similarly were prepared methylthiohydantoins of: aspartic acid, m. 176°; glutamic acid, m. 146°; asparagine, m. 187°; glutamine, m. 150°. Paper chromatographic mobilities of these were reported, as were the uv spectra.

=> s l1 and (cancer or tumor or neoplasm)
REG1stRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

```
SAMPLE SEARCH INITIATED 10:08:14 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      212 TO ITERATE

100.0% PROCESSED      212 ITERATIONS                                  0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:         3367 TO     5113
PROJECTED ANSWERS:               0 TO        0

L5            0 SEA SSS SAM L1



L6           0 L5


        396424 CANCER
         58330 CANCERS
        410926 CANCER
                 (CANCER OR CANCERS)
        487910 TUMOR
        179494 TUMORS
        542812 TUMOR
                 (TUMOR OR TUMORS)
        533486 NEOPLASM
         37759 NEOPLASMS
        550587 NEOPLASM
                 (NEOPLASM OR NEOPLASMS)
L7           0 L6 AND (CANCER OR TUMOR OR NEOPLASM)

=> file caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                      ENTRY    SESSION
FULL ESTIMATED COST                                    7.22     374.25

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                      ENTRY    SESSION
CA SUBSCRIBER PRICE                                    0.00     -27.88

FILE 'CAPLUS' ENTERED AT 10:08:20 ON 16 MAR 2009
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2009 AMERICAN CHEMICAL SOCIETY (ACS)
```



```
FILE COVERS 1907 - 16 Mar 2009  VOL 150 ISS 12
FILE LAST UPDATED: 15 Mar 2009  (20090315/ED)
```

Caplus now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2008.

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy.html

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s l2 and (cancer or tumor or neoplasm)
            34 L2
        396424 CANCER
         58330 CANCERS
        410926 CANCER
                 (CANCER OR CANCERS)
        487910 TUMOR
        179494 TUMORS
        542812 TUMOR
                 (TUMOR OR TUMORS)
        533486 NEOPLASM
         37759 NEOPLASMS
        550587 NEOPLASM
                 (NEOPLASM OR NEOPLASMS)
L8          12 L2 AND (CANCER OR TUMOR OR NEOPLASM)

=> d l8 ibib abs 1-12

L8   ANSWER 1 OF 12  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:        2008:1136027  CAPLUS
DOCUMENT NUMBER:         149:462087
TITLE:                   Structure-activity relationship study of a novel
                         necroptosis inhibitor, necrostatin-7
AUTHOR(S):               Zheng, Weihong; Degterev, Alexei; Hsu, Emily; Yuan,
                         Junying; Yuan, Chengye
CORPORATE SOURCE:        State Key Laboratory of Bio-Organic and Natural
                         Product Chemistry, Shanghai Institute of Organic
                         Chemistry, Chinese Academy of Sciences, Shanghai,
                         200032, Peop. Rep. China
SOURCE:                  Bioorganic & Medicinal Chemistry Letters (2008),
                         18(18), 4932-4935
                         CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER:               Elsevier Ltd.
DOCUMENT TYPE:           Journal
LANGUAGE:                English
AB   Necroptosis is a regulated caspase-independent cell death mechanism
     characterized by morphol. features resembling non-regulated necrosis.
     Necrotatin-7 (Nec-7), a novel potent small-mol. inhibitor of necroptosis,
     is structurally distinct from previously described necrostatins (Nec-1,
     Nec-3, Nec-4 and Nec-5).  Here, we describe a series of structural
     modifications and the structure-activity relationship (SAR) of the Nec-7
     series for inhibiting necroptosis.
REFERENCE COUNT:         18    THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8   ANSWER 2 OF 12  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:        2008:1021408  CAPLUS
DOCUMENT NUMBER:         150:206161
TITLE:                   Necrostatin-1 reduces histopathology and improves
                         functional outcome after controlled cortical impact in
                         mice
AUTHOR(S):               You, Zerong; Savitz, Sean I.; Yang, Jinsheng;
```

Degterev, Alexei; Yuan, Junying; Cuny, Gregory D.; Moskowitz, Michael A.; Whalen, Michael J.

CORPORATE SOURCE: Neuroscience Center, Massachusetts General Hospital, Harvard Medical School, Charlestown, MA, 02129, USA

SOURCE: Journal of Cerebral Blood Flow & Metabolism (2008), 28(9), 1564-1573
CODEN: JCBMDN; ISSN: 0271-678X
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Necroptosis is a newly identified type of programmed necrosis initiated by the activation of tumor necrosis factor alpha (TNFα)/Fas. Necrostatin-1 is a specific inhibitor of necroptosis that reduces ischemic tissue damage in exptl. stroke models. We previously reported decreased tissue damage and improved functional outcome after controlled cortical impact (CCI) in mice deficient in TNFα and Fas. Hence, we hypothesized that necrostatin-1 would reduce histopathol. and improve functional outcome after CCI in mice. Compared with vehicle-/inactive analog-treated controls, mice administered necrostatin-1 before CCI had decreased propidium iodide-pos. cells in the injured cortex and dentate gyrus (6 h), decreased brain tissue damage (days 14, 35), improved motor (days 1 to 7), and Morris water maze performance (days 8 to 14) after CCI. Improved spatial memory was observed even when drug was administered 15 mins after CCI. Necrostatin-1 treatment did not reduce caspase-3-pos. cells in the dentate gyrus or cortex, consistent with a known caspase-independent mechanism of necrostatin-1. However, necrostatin-1 reduced brain neutrophil influx and microglial activation at 48 h, suggesting a novel anti-inflammatory effect in traumatic brain injury (TBI). The data suggest that necroptosis plays a significant role in the pathogenesis of cell death and functional outcome after TBI and that necrostatin-1 may have therapeutic potential for patients with TBI. Journal of Cerebral Blood Flow & Metabolism (2008) 28, 1564-1573; doi:10.1038/jcbfm.2008.44; published online 21 May 2008.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2008:530303 CAPLUS
DOCUMENT NUMBER: 149:69718

TITLE: A key in vivo antitumor mechanism of action of natural product-based brassinins is inhibition of indoleamine 2,3-dioxygenase

AUTHOR(S): Banerjee, T.; DuHadaway, J. B.; Gaspari, P.; Sutanto-Ward, E.; Munn, D. H.; Mellor, A. L.; Malachowski, W. P.; Prendergast, G. C.; Muller, A. J.

CORPORATE SOURCE: NewLink Genetics Corporation, Ames, IA, USA

SOURCE: Oncogene (2008), 27(20), 2851-2857
CODEN: ONCNES; ISSN: 0950-9232
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Agents that interfere with tumoral immune tolerance may be useful to prevent or treat cancer. Brassinin is a phytoalexin, a class of natural products derived from plants that includes the widely known compound resveratrol. Brassinin has been demonstrated to have chemopreventive activity in preclin. models but the mechanisms underlying its anticancer properties are unknown. Here, we show that brassinin and a synthetic derivative 5-bromo-brassinin (5-Br-brassinin) are bioavailable inhibitors of indoleamine 2,3-dioxygenase (IDO), a pro-tolerogenic enzyme that drives immune escape in cancer. Like other known IDO inhibitors, both of these compds. combined with chemotherapy to elicit regression of autochthonous mammary gland tumors in MMTV-Neu mice.

Furthermore, growth of highly aggressive melanoma isograft tumors was suppressed by single agent treatment with 5-Br-brassinin. This response to treatment was lost in athymic mice, indicating a requirement for active host T-cell immunity, and in IDO-null knockout mice, providing direct genetic evidence that IDO inhibition is essential to the antitumor mechanism of action of 5-Br-brassinin. The natural product brassinin thus provides the structural basis for a new class of compds. with in vivo anticancer activity that is mediated through the inhibition of IDO.
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2008:421553 CAPLUS
DOCUMENT NUMBER: 149:298787
TITLE: Down-regulation of the indoleamine 2, 3-dioxygenase (IDO) transcription by tryptophan analogues
AUTHOR(S): Okamoto, Takeaki; Tone, Shigenobu; Kanoichi, Hiroaki; Ohyama, Fumio; Minatogawa, Yohsuke
CORPORATE SOURCE: Department of Biochemistry, Kawasaki Medical School, 577 Matsushima, Kurashiki, Okayama, 701-0192, Japan
SOURCE: International Congress Series (2007), 1304(Interdisciplinary Conference on Tryptophan and Related Substances: Chemistry, Biology, and Medicine, 2006), 352-356
CODEN: EXMDA4; ISSN: 0531-5131
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Indoleamine 2,3-dioxygenase (IDO; EC 1.13.11.42) is a rate-limiting enzyme involved in the catabolism of tryptophan, which is an essential amino acid. It is induced under pathol. conditions, such as the presence of viral infections or tumor cells. This enzyme is induced by IFN-γ in the mouse rectal carcinoma cell line CMT-93. It is known that both 1-methyl-L-tryptophan (1-MT) and methylthiohydantoin-DL-tryptophan (MTH-trp) are tryptophan analogs, and are authentic inhibitors of the enzymic activity of IDO. In this study, we examined the effects of both 1-MT and MTH-trp on the IFN-γ inducible IDO expression of CMT-93. As a result, the IFN-γ inducible IDO mRNA and the protein levels in CMT-93 were suppressed by 1-MT and MTH-trp, independently. Moreover, tryptophan (Trp), as a substrate of IDO, also suppressed IDO induction by IFN-γ at the transcriptional level. These results suggest that 1-MT and MTH-trp as inhibitors of IDO enzymic activity, and Trp suppress IDO induction by IFN-γ at the transcriptional level.
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:830612 CAPLUS
DOCUMENT NUMBER: 148:282740
TITLE: Transcriptional regulation of indoleamine 2,3-dioxygenase (IDO) by tryptophan and its analogue
AUTHOR(S): Okamoto, Takeaki; Tone, Shigenobu; Kanouchi, Hiroaki; Miyawaki, Chie; Ono, Sayuri; Minatogawa, Yohsuke
CORPORATE SOURCE: Department of Biochemistry, Kawasaki Medical School, 577 Matsushima, Kurashiki, Okayama, 701-0192, Japan
SOURCE: Cytotechnology (2007), 54(2), 107-113
CODEN: CYTOER; ISSN: 0920-9069
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Indoleamine 2,3-dioxygenase (IDO; EC 1.13.11.42) is a rate-limiting enzyme

involved in the catabolism of tryptophan, which is an essential amino acid. It is induced under pathol. conditions, such as the presence of viral infections or tumor cells. This enzyme is induced by IFN-γ in the mouse rectal carcinoma cell line CMT-93. It is known that both 1-methyl-l-tryptophan (1-MT) and methylthiohydantoin-dl-tryptophan (MTH-trp) are tryptophan analogs, and are authentic inhibitors of the enzymic activity of IDO. In this study, we examined the effects of both 1-MT and MTH-trp on the IFN-γ inducible IDO expression of CMT-93. As a result, the IFN-γ inducible IDO mRNA and the protein levels in CMT-93 were suppressed by 1-MT and MTH-trp, independently. Moreover, tryptophan (Trp), as a substrate of IDO, also suppressed IDO induction by IFN-γ at the transcriptional level. These results suggest that 1-MT and MTH-trp are as inhibitors of IDO enzymic activity, and Trp suppresses IDO induction by IFN-γ at the transcriptional level.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2007:730236 CAPLUS

DOCUMENT NUMBER: 147:143418

TITLE: Benzo[g]indazole, indole and tetralone compounds and their preparation, screening, and methods of treatment of diseases caused by TNFα or RIP1 protein

INVENTOR(S): Yuan, Junying; Degterev, Alexei; Hitomi, Junichi; Cuny, Gregory D.; Jagtap, Prakash

PATENT ASSIGNEE(S): President and Fellows of Harvard College, USA; The Brigham and Women's Hospital, Inc.

SOURCE: PCT Int. Appl., 263pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

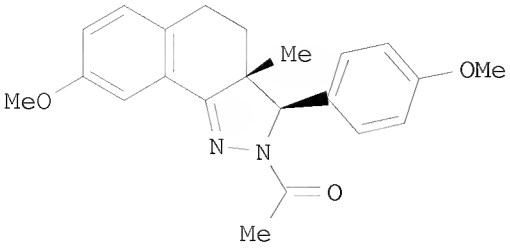
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007075772	A2	20070705	WO 2006-US48583	20061220
WO 2007075772	A3	20090219		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
AU 2006331754	A1	20070705	AU 2006-331754	20061220
AU 2006331754	A2	20080814		
CA 2633500	A1	20070705	CA 2006-2633500	20061220
EP 1968583	A2	20080917	EP 2006-847822	20061220
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS				

PRIORITY APPLN. INFO.:	US 2005-751913P	P	20051220
	US 2006-843304P	P	20060908
	WO 2006-US48583	W	20061220

GI



I

AB The invention features compds., pharmaceutical compns., and methods for treating trauma, ischemia, stroke, degenerative diseases associated with cellular necrosis, and other conditions. Screening assays for identifying compds. useful for treating these conditions are also described. Example compound I was prepared by a multistep procedure (procedure given). All the invention compds. were evaluated for their necrosis inhibitory activity and their structure-activity relationship.

L8 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:337477 CAPLUS
DOCUMENT NUMBER: 146:408284
TITLE: Application of alkannin to prepare medicine inducing cytoclasis programmed death
INVENTOR(S): Hu, Xun; Han, Weidong
PATENT ASSIGNEE(S): Zhejiang University, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 20pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1931152	A	20070321	CN 2006-10053627	20060927

PRIORITY APPLN. INFO.: CN 2006-10053627 20060927

AB The patent relates to application of alkannin((+)-5,8-dihydroxy-2-(1-hydroxy-4-methyl-3-pentenyl)-1,4-naphthoquinone) to prepare medicine(liquid prepns., granules, tablets, medicinal instant granules, gelatin pills, capsules, sustained-release preparation, dripping pills or injections) inducing cytoclasis programmed death, and the medicine is composed of alkannin and medical excipient or carrier. The alkannin can kill multidrug resistance tumor cells, and has low toxicity.

L8 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:157223 CAPLUS
DOCUMENT NUMBER: 147:65087
TITLE: Chemical genetic approaches to probing cell death
AUTHOR(S): Gangadhar, Nidhi M.; Stockwell, Brent R.
CORPORATE SOURCE: Department of Biological Sciences, 614 Fairchild Center, New York, NY, 10027, USA
SOURCE: Current Opinion in Chemical Biology (2007), 11(1), 83-87
CODEN: COCBF4; ISSN: 1367-5931
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Chemical genetics has arisen as a tool for the discovery of pathways and proteins in mammalian systems. This approach, comprising small-mol. screening combined with biochem. and genomic target identification methods, enables one to assess which proteins are involved in regulating a particular phenotype. Applied to cell death, this strategy can reveal novel targets and pathways regulating the demise of mammalian cells. Numerous diseases have been linked to the loss of regulation of cell death. Defining the mechanisms governing cell death in these diseases might lead to the discovery of therapeutic agents and targets and provide a richer understanding of the mortality of living systems. Recent advances include the discovery of novel small mols. regulating cell death pathways - necrostatin and erastin - as well as the elucidation of the mechanism of death induced in cancer cells by the cytotoxic agent Apratoxin A.

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:369265 CAPLUS

DOCUMENT NUMBER: 142:423892

TITLE: Alanyl aminopeptidase inhibitors for functionally influencing different cells and treating immunological, inflammatory, neuronal, and other diseases

INVENTOR(S): Ansorge, Siegfried; Bank, Ute; Nordhoff, Karsten; Tager, Michael; Striggow, Frank

PATENT ASSIGNEE(S): Institut Fur Medizintechnologie Magdeburg GmbH IMTM, Germany; Keyneurotek AG

SOURCE: PCT Int. Appl., 332 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005037257	A2	20050428	WO 2004-EP11643	20041015
WO 2005037257	A3	20060914		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10348023	A1	20050519	DE 2003-10348023	20031015
AU 2004281536	A1	20050428	AU 2004-281536	20041015
CA 2542723	A1	20050428	CA 2004-2542723	20041015
EP 1673075	A2	20060628	EP 2004-790485	20041015
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
CN 1897928	A	20070117	CN 2004-80036456	20041015
JP 2007508349	T	20070405	JP 2006-534706	20041015
US 20070037752	A1	20070215	US 2006-575882	20060915

PRIORITY APPLN. INFO.: DE 2003-10348023 A 20031015
WO 2004-EP11643 W 20041015

OTHER SOURCE(S): MARPAT 142:423892

AB The invention discloses substances which specifically inhibit peptidases splitting ala-p-nitroanilide for use in medicine. The invention further discloses the use of at least one such substance or at least one pharmaceutical or cosmetic composition containing such a substance for preventing and treating diseases, especially diseases with an overshooting immune response (autoimmune diseases, allergies, and transplant rejections), other chronic inflammatory diseases, neuronal diseases, brain damage, skin diseases (acne and psoriasis, among others), tumors, and special viral infections (including SARS).

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:927197 CAPLUS

DOCUMENT NUMBER: 141:388648

TITLE: Novel ido (indoleamine 2,3-dioxygenase) inhibitors and methods of use

INVENTOR(S): Prendergast, George C.; Muller, Alexander J.; Duhadaway, James B.; Malachowski, William

PATENT ASSIGNEE(S): Lankenau Institute for Medical Research, USA

SOURCE: PCT Int. Appl., 115 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004094409	A1	20041104	WO 2004-US5154		20040220
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2520586	A1	20041104	CA 2004-2520586		20040220
EP 1606285	A1	20051221	EP 2004-713430		20040220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
CN 1795187	A	20060628	CN 2004-80008331		20040220
CN 1794986	A	20060628	CN 2004-80014321		20040220
JP 2006521377	T	20060921	JP 2006-508788		20040220
CN 101265254	A	20080917	CN 2008-10092243		20040220
CN 101265259	A	20080917	CN 2008-10092244		20040220
US 20070173524	A1	20070726	US 2006-550444		20060601
PRIORITY APPLN. INFO.:			US 2003-458162P	P	20030327
			US 2003-527449P	P	20031205
			CN 2004-80008331	A3	20040220
			WO 2004-US5154	W	20040220

OTHER SOURCE(S): MARPAT 141:388648

AB Novel inhibitors of indoleamine 2,3-dioxygenase (IDO) activity are provided. In yet another embodiment of the present invention, a combination treatment protocol comprising administration of an IDO inhibitor with a signal transduction inhibitor (STI) or chemotherapeutic agent is provided, which is effective for suppressing tumor growth. In still another embodiment of the present invention, a

combination treatment protocol is provided for the treatment of a chronic viral infection, comprising the administration of an IDO inhibitor and a chemotherapeutic agent.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:927043 CAPLUS
DOCUMENT NUMBER: 141:388646
TITLE: Novel methods for the treatment of cancer and viral infections
INVENTOR(S): Prendergast, George C.; Muller, Alexander J.; Duhadaway, James B.; Malachowski, William
PATENT ASSIGNEE(S): Lankenau Institute for Medical Research, USA
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004093871	A1	20041104	WO 2004-US5155		20040220
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2520172	A1	20041104	CA 2004-2520172		20040220
EP 1613308	A1	20060111	EP 2004-713378		20040220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
CN 1795187	A	20060628	CN 2004-80008331		20040220
CN 1794986	A	20060628	CN 2004-80014321		20040220
JP 2006521378	T	20060921	JP 2006-508789		20040220
CN 101265254	A	20080917	CN 2008-10092243		20040220
CN 101265259	A	20080917	CN 2008-10092244		20040220
US 20070099844	A1	20070503	US 2006-551151		20060518
PRIORITY APPLN. INFO.:			US 2003-458162P	P	20030327
			US 2003-527449P	P	20031205
			CN 2004-80008331	A3	20040220
			WO 2004-US5155	W	20040220

AB Compns. and methods for the treatment of malignancy and chronic viral infection are disclosed. A method is claimed for treating a cancer comprising administering at least one indoleamine 2,3-dioxygenase (IDO) inhibitor and at least one signal transduction inhibitor (STI). A method is claimed for treating a cancer comprising administering at least one immunomodulator, other than IDO inhibitor, and at least one cytotoxic chemotherapeutic agent or at least one STI. A method for treating a chronic viral infection in a patient is claimed comprising administering at least one IDO inhibitor and at least one chemotherapeutic agent. Pharmaceutical compns. containing compds. of the invention for treating cancer and viral infections are also claimed.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2001:300459 CAPLUS
DOCUMENT NUMBER: 134:320879
TITLE: Small molecule inhibitors of necrosis
INVENTOR(S): Yuan, Junying; Degterev, Alexei; Mitchison, Timothy
PATENT ASSIGNEE(S): President and Fellows of Harvard College, USA
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001028493	A2	20010426	WO 2000-US28475	20001013
WO 2001028493	A3	20010607		
W: CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6756394	B1	20040629	US 2000-688015	20001013
US 20050131044	A1	20050616	US 2004-880377	20040629
US 7253201	B2	20070807		

PRIORITY APPLN. INFO.: US 1999-159668P P 19991015
US 2000-174749P P 20000106
US 2000-688015 A1 20001013
OTHER SOURCE(S): MARPAT 134:320879
AB The invention features methods for decreasing necrosis. The invention also features methods for treating a subject with a condition in which necrosis occurs. The invention further features chemical compds. used to decrease necrosis.
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> file registry

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	51.72	425.97

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-9.84	-37.72

FILE 'REGISTRY' ENTERED AT 10:19:16 ON 16 MAR 2009
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2009 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 13 MAR 2009 HIGHEST RN 1120564-02-4
DICTIONARY FILE UPDATES: 13 MAR 2009 HIGHEST RN 1120564-02-4

New CAS Information Use Policies, enter HELP USAGETERMS for details.

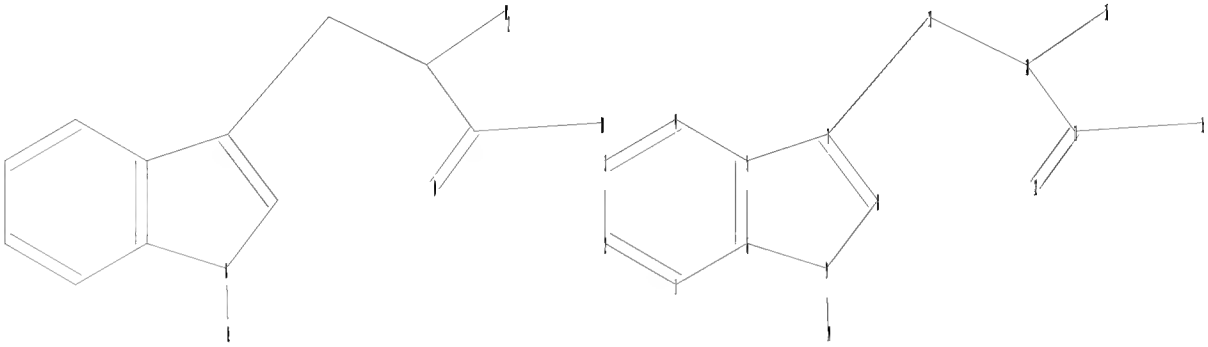
TSCA INFORMATION NOW CURRENT THROUGH January 9, 2009.

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\STNEXP\Queries\10551151a.str

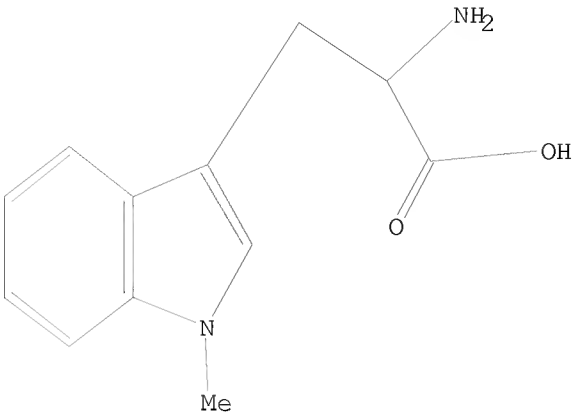


chain nodes :
10 11 12 13 14 15 16
ring nodes :
1 2 3 4 5 6 7 8 9
chain bonds :
7-13 9-14 10-13 10-11 10-16 11-12 11-15
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9
exact/norm bonds :
5-7 6-9 7-8 8-9 10-16
exact bonds :
7-13 9-14 10-13 10-11
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 11-12 11-15

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS

L9 STRUCTURE UPLOADED

=> d l9
L9 HAS NO ANSWERS
L9 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l9 fam ful
FULL SEARCH INITIATED 10:19:41 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 450 TO ITERATE

100.0% PROCESSED 450 ITERATIONS 8 ANSWERS
SEARCH TIME: 00.00.01

L10 8 SEA FAM FUL L9

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	73.33	499.30

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-37.72

FILE 'CAPLUS' ENTERED AT 10:19:46 ON 16 MAR 2009

FILE COVERS 1907 - 16 Mar 2009 VOL 150 ISS 12
FILE LAST UPDATED: 15 Mar 2009 (20090315/ED)

Caplus now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2008.

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy.html

This file contains CAS Registry Numbers for easy and accurate
substance identification.

```
=> s l0 and (cancer? or tumor? or tumour? or neoplasm?)
          3512 L0
        415443 CANCER?
        556187 TUMOR?
          5683 TUMOUR?
        550694 NEOPLASM?
L11         47 L0 AND (CANCER? OR TUMOR? OR TUMOUR? OR NEOPLASM?)

=> s l11 and cisplatin
         25241 CISPLATIN
            10 CISPLATINS
         25243 CISPLATIN
                 (CISPLATIN OR CISPLATINS)
L12          5 L11 AND CISPLATIN

=> d l12 ibib abs 1-5

L12  ANSWER 1 OF 5  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:        2006:679547  CAPLUS
DOCUMENT NUMBER:         146:287764
TITLE:                   Study on the anti-proliferation effect of curcumin
                         combined with cisplatin on the human lung
                         cancer cell line A549 in vitro
AUTHOR(S):               Cui, Jiandong; Hu, Yide
CORPORATE SOURCE:        PLA Cancer Center of Xinqiao Hospital, The Third
                         Military Med. Univ., Chongqing, 400037, Peop. Rep.
                         China
SOURCE:                  Sichuan Yixue (2006), 27(1), 1-3
                         CODEN: SYIIAO; ISSN: 1004-0501
PUBLISHER:               Sichuan Yixue Bianjibu
DOCUMENT TYPE:           Journal
LANGUAGE:                Chinese
AB   The objective is to investigate the anti-proliferation effect of curcumin
     combined with cisplatin on the human lung cancer cell
     line A549 in vitro.  MTT was used to measure inhibitory effects of
     curcumin and cisplatin on growth of A549 cells.  Curcumin and
     cisplatin inhibited the growth of the human lung cancer
     cell line A549 in a concentration-and time-dependent manner, their IC50 were
18.4
     μmol/L, 0.966μg/mL resp.  Compared with either curcumin or
     cisplatin alone, combining curcumin at l0.mu.mol/L,
     15μmol/L, 20μmol/L with   cisplatin at 1μg/mL, 2μg/mL
     resp. increased the growth inhibition rate of A549 cells (P<0.05)
     significantly, suggesting synergistic actions of the two drugs.  Curcumin
     could significantly inhibit the growth of A549 cells, which increases the
     sensitivity of A549 cells to cisplatin.

L12  ANSWER 2 OF 5  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:        2004:208221  CAPLUS
DOCUMENT NUMBER:         141:64542
TITLE:                   Interaction of inhibiting effect of cyclooxygenase-2
                         and anticancer drugs on nasopharyngeal carcinoma
                         strains
AUTHOR(S):               Chen, Peiyi; Long, Qicai
CORPORATE SOURCE:        Department of Clinical Pharmacology, School of
```

Pharmaceutical Sciences, Sun Yat-sen University, Guangzhou, 510080, Peop. Rep. China
SOURCE: Zhongguo Linchuang Yaolixue Zazhi (2002), 18(6), 425-430
CODEN: ZLYZE9; ISSN: 1001-6821
PUBLISHER: Beijing Yike Daxue, Linchuang Yaoli Yanjiuso
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB The interaction of inhibiting effects of cyclooxygenase- 2 inhibitors and anticancer drugs on nasopharyngeal carcinoma (NPC) cells was studied. Inhibiting action of COX-2 inhibitors and cytotoxic drugs on NPC strains (CNE1, CNE2, SUNE) was observed by MTT assay. Interaction of COX-2 inhibitors and anticancer drugs was estimated by S-N-K statistic anal. and q value provided by Jun Zheng-jun's method. Synergistic effects showed in inhibiting action of CNE1 strain after dosing Nim (nimesulide) 25 μmol/L-1 BLM 0.5, 1, 2 mg/L-1, Nim μmol/L-1/CDDP (cisplatin) 6.25, 12.5 mg/L-1, and Nim 25 μmol/L-1/VCR 1 mg/L-1.n. Inhibiting rates for CNE1 strain were 33%, 47%, 48%, 59%, 63%, and 32%, resp. (compared with single drugs, P<0.05 or P < 0.01); q value: 1.88, 2.54, 1.65, 2.70, 1.37, and 1.45, resp. Antagonism manifested in inhibiting action of CNE2 strain after dosing Nim 25 μmol/L-1/CDDP 1, 2.5 mg/L-1; inhibiting rates for CNE2 strain were 33% or 25%, resp. (compared with single drug, P < 0.05 or P < 0.01, q: 0.69 and 0.32). Antagonism in inhibiting action of SUNE strain exhibited in Nim 25 μmol/L-1/CDDP 6.25, 12.5 mg/L-1, inhibiting rates for SUNE strain were 21% or 17%, resp. (compared with single drug, P,<,0.05 or P,<,0.01), q value: 0.50 and 0.21, resp. Synergistic effect represented in inhibiting action of CNE1 strain after dosing Cel (celecoxib) 2.5 μmol/L-1/BLM 1.2 mg/L-1, Cel 2.5 μmol/L-1/CDDP 12.5 mg/L-1, Cel 2.5 μmol/L-1/VCR 1 mg/ L0-1, inhibiting rates for CNE1 strain were 43%, 58%, 50%, 39%, resp. (compared with single drug, P < 0.05 or P < 0.01), q value: 1.59, 1.61, 1.43, 1.49, resp. Additivity effect appeared in inhibiting action of SUNE strain after dosing Cel 2.5 μmol L-1/BLM 0.5 mg/L-1 or CDDP 6.25 mg/L-1, inhibiting rates for CNE1 strain were 29%, 23%, resp. (compared with single drug, P < 0.05 or P < 0.01), q value: 1.11, 1.02, resp. Synergistic effect represented in inhibiting action of SUNE strain after dosing Cel 2.5 μmol/L-1/BLM 1.2 mg/L-1 or CDDP 6.25 mg/L-1 or 12.5 mg/L-1, inhibiting rates for SUNE strain were 16%, 60%, 19%, 48%, resp. (compared with single drug, P < 0.05 or P < 0.01) q value: 1.45, 1.91, 1.23, 1.57, resp. Synergism or additivity of inhibition to CNE1 strain caused by combination dosing of nimesulide with BLM or CDDP or VCR, whereas antagonism of inhibition to CNE2 and SUNE strains was seen in combination dosing of nimesulide with CDDP. Synergism or additivity of inhibition to CNE1 and SUNE strains showed in concomitance of celecoxib with BLM, or CDDP, or VCR.

L12 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2001:482608 CAPLUS
DOCUMENT NUMBER: 135:338799
TITLE: Glutathione-dependent binding of a photoaffinity analog of agosterol A to the C-terminal half of human multidrug resistance protein
AUTHOR(S): Ren, Xiao-Qin; Furukawa, Tatsuhiko; Aoki, Shunji; Nakajima, Tatsuo; Sumizawa, Tomoyuki; Haraguchi, Misako; Chen, Zhe-Sheng; Kobayashi, Motomasa; Akiyama, Shin-Ichi
CORPORATE SOURCE: Department of Cancer Chemotherapy, Institute for Cancer Research, Faculty of Medicine, Kagoshima University, Kagoshima, 890-8520, Japan
SOURCE: Journal of Biological Chemistry (2001), 276(25), 23197-23206
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB MRP1 is a 190-kDa membrane glycoprotein that confers multidrug resistance (MDR) to tumor cells. MRP1 is characterized by an N-terminal transmembrane domain (TMD0), which is connected to a P-glycoprotein-like core region (ΔMRP) by a cytoplasmic linker domain zero (L0). It has been demonstrated that GSH plays an important role in MRP1-mediated MDR. However, the mechanism by which GSH mediates MDR and the precise roles of TMD0 and L0 are not known. We synthesized [125I]11-azidophenyl agosterol A ([125I]azidoAG-A), a photoaffinity analog of the MDR-reversing agent, agosterol A (AG-A), to photolabel MRP1, and found that the analog photolabeled the C-proximal mol. of MRP1 (C932-1531) in a manner that was GSH-dependent. The photolabeling was inhibited by anticancer agents, reversing agents and leukotriene C4. Based on photolabeling studies in the presence and absence of GSH using membrane vesicles expressing various truncated, co-expressed, and mutated MRP1s, we found that L0 is the site on MRP1 that interacts with GSH. This study demonstrated that GSH is required for the binding of an unconjugated agent to MRP1 and suggested that GSH interacts with L0 of MRP1. The photoanalog of AG-A will be useful for identifying the drug binding site within MRP1, and the role of GSH in transporting substrates by MRP1.
REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1996:59879 CAPLUS
DOCUMENT NUMBER: 124:164564
ORIGINAL REFERENCE NO.: 124:30203a,30206a
TITLE: Collateral sensitivity to radiation and cisplatin in a multidrug-resistant human leukemia cell line
AUTHOR(S): Cho, Jonathan; Lee, Young; Lutzky, Jose; Redpath, Leslie; Slater, Lewis
CORPORATE SOURCE: Dep. Medicine Radiation Oncol., Univ. California, Irvine, CA, USA
SOURCE: Cancer Chemotherapy and Pharmacology (1995), 37(1/2), 168-72
CODEN: CCPHDZ; ISSN: 0344-5704
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Although collateral sensitivity to gamma radiation has previously been described in multidrug-resistant tumor cell lines, we describe here a multidrug-resistant human T-cell acute lymphatic leukemia cell line, L1000, which displayed increased sensitivity to both gamma radiation and cisplatin. Cisplatin cytotoxicity of parental L0 cells L100 cells was enhanced, whereas radiation sensitivity of L0 and L100 cells was unaltered by glutathione depletion. These results indicate that disparate mechanism are operative in the collateral sensitivity of L100 cells to gamma radiation and cisplatin.

L12 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1991:505609 CAPLUS
DOCUMENT NUMBER: 115:105609
ORIGINAL REFERENCE NO.: 115:17905a,17908a
TITLE: Differential in vitro sensitivity of human tumor and normal cells to chemotherapeutic agents and resistance modulators
AUTHOR(S): Nygren, Peter; Larsson, Rolf
CORPORATE SOURCE: Dep. Oncol., Univ. Hosp., Uppsala, S-751 85, Swed.

SOURCE: International Journal of Cancer (1991), 48(4), 598-604
CODEN: IJCNAW; ISSN: 0020-7136
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The intrinsically vincristine(Vcr)-resistant human kidney adenocarcinoma cell line ACHN, the human acute lymphoblastic leukemia cell line L0, its more-than-100-fold Vcr-resistant subline L100, normal human fibroblasts and lymphocytes, also tumor cells from patients with chronic lymphocytic leukemia (CLL), acute myeloblastic leukemia (AML) and solid tumors, were compared for sensitivity to cytotoxic drugs and resistance modulators (RMs). The L100 cells showed pronounced sensitivity to the RMs verapamil (Ver), cyclosporin A (CsA) and buthionine sulfoximine (BSO) alone as well as to cisplatin, whereas the L0 and ACHN cells, also slowly growing fibroblasts and non-proliferating lymphocytes, were considerably less sensitive. Compared with AML cells and lymphocytes, CLL cells were more sensitive to Ver and CsA alone. The cytotoxicity of Vcr was increased in the Vcr-resistant ACHN and L100, but also in sensitive L0 cells by Ver and CsA, with smaller effects on Dox and Vp-16 toxicity. Fibroblasts and lymphocytes were generally resistant to the cytotoxic agents and RM addition had only minor effects. CLL cells were more sensitive to Dox and Vcr as compared with normal lymphocytes, with potentiation of the Vcr effect by Ver and CsA. The Vcr effect in non-proliferating Vcr-resistant cells from a malignant schwannoma was potentiated by Ver and CsA, which had no effect in cells from a kidney adenocarcinoma. Cytotoxicity of RMs alone is not dependent on the proliferation rate of tumor cells and that potentiation of cytotoxic drugs by RMs may be selective for tumor cells irresp. of their initial level and mode of drug resistance.

```
=> s l10 and (cancer? or tumor? or tumour? or neoplasm?)
           205 L10
        415443 CANCER?
        556187 TUMOR?
          5683 TUMOUR?
        550694 NEOPLASM?
L13         35 L10 AND (CANCER? OR TUMOR? OR TUMOUR? OR NEOPLASM?)

=> s l13 and cisplatin
         25241 CISPLATIN
            10 CISPLATINS
         25243 CISPLATIN
                (CISPLATIN OR CISPLATINS)
L14          5 L13 AND CISPLATIN

=> d l14 ibib abs 1-5

L14 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:        2006:1157586 CAPLUS
DOCUMENT NUMBER:         145:465678
TITLE:                   Compositions and methods for cancer
                         immunotherapy
INVENTOR(S):             Rossignol, Daniel P.; Ishizaka, Sally T.; Hawkins,
                         Lynn D.; Fields, Scott
PATENT ASSIGNEE(S):      Eisai Co., Ltd, Japan
SOURCE:                  PCT Int. Appl., 85pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  2
PATENT INFORMATION:
```

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006116423	A2	20061102	WO 2006-US15668	20060426
WO 2006116423	A3	20081009		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
AU 2006241206	A1	20061102	AU 2006-241206	20060426
CA 2605749	A1	20061102	CA 2006-2605749	20060426
EP 1874342	A2	20080109	EP 2006-751398	20060426
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
JP 2008539249	T	20081113	JP 2008-509049	20060426
KR 2007122510	A	20071231	KR 2007-724654	20071026
CN 101355928	A	20090128	CN 2006-80014380	20071026
PRIORITY APPLN. INFO.:			US 2005-674680P P	20050426
			WO 2006-US15668 W	20060426

AB The invention relates to immunotherapeutic compds., mainly TLR agonists, tumor vaccines, and therapeutic antibodies, and methods for stimulating an immune response in an individual at risk for developing cancer, diagnosed with a cancer, in treatment for cancer, or in post-therapy recovery from cancer. Also, the compds. of the invention can be administered as a prophylactic to an individual to prevent or delay the development of cancer.

L14 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:1019533 CAPLUS
DOCUMENT NUMBER: 141:420433
TITLE: Use of inhibitors of indoleamine-2,3-dioxygenase in combination with other therapeutic modalities in the treatment of cancer and infection
INVENTOR(S): Munn, David; Mellor, Andrew
PATENT ASSIGNEE(S): Medical College of Georgia Research Institute, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 42 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20040234623	A1	20041125	US 2004-780797	20040217
US 20050186289	A1	20050825	US 2004-780150	20040217
PRIORITY APPLN. INFO.:			US 2003-459489P P	20030401
			US 2004-538647P P	20040122

AB The invention discloses a method for treating a subject with a cancer or an infection, the method including administering an inhibitor of indoleamine-2,3-dioxygenase (IDO) in an amount effective to reverse IDO-mediated immunosuppression, and administering at least one

addnl. therapeutic agent, wherein the administration of the inhibitor of IDO and the at least one addnl. therapeutic agent demonstrate therapeutic synergy.

L14 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:927197 CAPLUS
DOCUMENT NUMBER: 141:388648
TITLE: Novel ido (indoleamine 2,3-dioxygenase) inhibitors and methods of use
INVENTOR(S): Prendergast, George C.; Muller, Alexander J.; Duhadaway, James B.; Malachowski, William
PATENT ASSIGNEE(S): Lankenau Institute for Medical Research, USA
SOURCE: PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004094409	A1	20041104	WO 2004-US5154		20040220
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2520586	A1	20041104	CA 2004-2520586		20040220
EP 1606285	A1	20051221	EP 2004-713430		20040220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
CN 1795187	A	20060628	CN 2004-80008331		20040220
CN 1794986	A	20060628	CN 2004-80014321		20040220
JP 2006521377	T	20060921	JP 2006-508788		20040220
CN 101265254	A	20080917	CN 2008-10092243		20040220
CN 101265259	A	20080917	CN 2008-10092244		20040220
US 20070173524	A1	20070726	US 2006-550444		20060601
PRIORITY APPLN. INFO.:			US 2003-458162P	P	20030327
			US 2003-527449P	P	20031205
			CN 2004-80008331	A3	20040220
			WO 2004-US5154	W	20040220

OTHER SOURCE(S): MARPAT 141:388648
AB Novel inhibitors of indoleamine 2,3-dioxygenase (IDO) activity are provided. In yet another embodiment of the present invention, a combination treatment protocol comprising administration of an IDO inhibitor with a signal transduction inhibitor (STI) or chemotherapeutic agent is provided, which is effective for suppressing tumor growth. In still another embodiment of the present invention, a combination treatment protocol is provided for the treatment of a chronic viral infection, comprising the administration of an IDO inhibitor and a chemotherapeutic agent.
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:927043 CAPLUS
DOCUMENT NUMBER: 141:388646

TITLE: Novel methods for the treatment of cancer and viral infections
INVENTOR(S): Prendergast, George C.; Muller, Alexander J.; Duhadaway, James B.; Malachowski, William
PATENT ASSIGNEE(S): Lankenau Institute for Medical Research, USA
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004093871	A1	20041104	WO 2004-US5155		20040220
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2520172	A1	20041104	CA 2004-2520172		20040220
EP 1613308	A1	20060111	EP 2004-713378		20040220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
CN 1795187	A	20060628	CN 2004-80008331		20040220
CN 1794986	A	20060628	CN 2004-80014321		20040220
JP 2006521378	T	20060921	JP 2006-508789		20040220
CN 101265254	A	20080917	CN 2008-10092243		20040220
CN 101265259	A	20080917	CN 2008-10092244		20040220
US 20070099844	A1	20070503	US 2006-551151		20060518
PRIORITY APPLN. INFO.:			US 2003-458162P	P	20030327
			US 2003-527449P	P	20031205
			CN 2004-80008331	A3	20040220
			WO 2004-US5155	W	20040220

AB Compns. and methods for the treatment of malignancy and chronic viral infection are disclosed. A method is claimed for treating a cancer comprising administering at least one indoleamine 2,3-dioxygenase (IDO) inhibitor and at least one signal transduction inhibitor (STI). A method is claimed for treating a cancer comprising administering at least one immunomodulator, other than IDO inhibitor, and at least one cytotoxic chemotherapeutic agent or at least one STI. A method for treating a chronic viral infection in a patient is claimed comprising administering at least one IDO inhibitor and at least one chemotherapeutic agent. Pharmaceutical compns. containing compds. of the invention for treating cancer and viral infections are also claimed.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1991:220909 CAPLUS
DOCUMENT NUMBER: 114:220909
ORIGINAL REFERENCE NO.: 114:37013a,37016a
TITLE: Investigations on the antiproliferative effects of amino acid antagonists targeting for aminoacyl-tRNA synthetases. Part III. Combination experiments
AUTHOR(S): Laske, Reiner; Schoenenberger, Helmut; Holler,

	Eggehard
CORPORATE SOURCE:	Inst. Pharm., Univ. Regensburg, Regensburg, D-8400, Germany
SOURCE:	Archiv der Pharmazie (Weinheim, Germany) (1991), 324(3), 153-60 CODEN: ARPMAS; ISSN: 0365-6233
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB The combined effects of amino acid antagonists with proven or potential inhibitory activities on aminoacyl-tRNA synthetases were investigated on the murine leukemic cell line P388 D1. As the best result a summation of the antiproliferative effects was observed Combinations with established cytostatic agents like platinum complexes or other antitumor compds. also yielded partly additive effects. In expts. performed with asparaginase, L-aspartic acid-β-hydroxamate gave synergistic growth inhibition of P388 D1 cells in vitro, which was reflected by additive effects against murine leukemia P388 in vivo.

=>

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	69.14	568.44

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-8.20	-45.92

STN INTERNATIONAL LOGOFF AT 10:37:15 ON 16 MAR 2009

Connecting via Winsock to STN

Welcome to STN International! Enter x:X

LOGINID:ssptacrs1614

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS	1		Web Page for STN Seminar Schedule - N. America
NEWS	2	AUG 10	Time limit for inactive STN sessions doubles to 40 minutes
NEWS	3	AUG 18	COMPENDEX indexing changed for the Corporate Source

(CS) field
NEWS 4 AUG 24 ENCOMPLIT/ENCOMPLIT2 reloaded and enhanced
NEWS 5 AUG 24 CA/CAplus enhanced with legal status information for U.S. patents
NEWS 6 SEP 09 50 Millionth Unique Chemical Substance Recorded in CAS REGISTRY
NEWS 7 SEP 11 WPIDS, WPINDEX, and WPIX now include Japanese FTERM thesaurus
NEWS 8 OCT 21 Derwent World Patents Index Coverage of Indian and Taiwanese Content Expanded
NEWS 9 OCT 21 Derwent World Patents Index enhanced with human translated claims for Chinese Applications and Utility Models
NEWS 10 OCT 27 Free display of legal status information in CA/CAplus, USPATFULL, and USPAT2 in the month of November.

NEWS EXPRESS MAY 26 09 CURRENT WINDOWS VERSION IS V8.4,
AND CURRENT DISCOVER FILE IS DATED 06 APRIL 2009.

NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS LOGIN Welcome Banner and News Items

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN customer agreement. This agreement limits use to scientific research. Use for software development or design, implementation of commercial gateways, or use of CAS and STN data in the building of commercial products is prohibited and may result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 10:01:30 ON 03 NOV 2009

=> file registry

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.22	0.22

FILE 'REGISTRY' ENTERED AT 10:01:51 ON 03 NOV 2009
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 1 NOV 2009 HIGHEST RN 1190833-66-9
DICTIONARY FILE UPDATES: 1 NOV 2009 HIGHEST RN 1190833-66-9

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 26, 2009.

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information

on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

```
=> e brassinin
E1          85     BRASSIN/BI
E2           2     BRASSINAZOLE/BI
E3          18 --> BRASSININ/BI
E4          19     BRASSININE/BI
E5          84     BRASSINOL/BI
E6          80     BRASSINOLIDE/BI
E7           3     BRASSINON/BI
E8           3     BRASSINONE/BI
E9          87     BRASSINOSTEROID/BI
E10          1     BRASSIODO/BI
E11          1     BRASSIODOL/BI
E12          5     BRASSIOPHOENIX/BI

=> s e3
L1          18 BRASSININ/BI

=> file caplus medline biosis embase
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                     ENTRY    SESSION
FULL ESTIMATED COST                                   5.83       6.05

FILE 'CAPLUS' ENTERED AT 10:02:26 ON 03 NOV 2009
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2009 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'MEDLINE' ENTERED AT 10:02:26 ON 03 NOV 2009

FILE 'BIOSIS' ENTERED AT 10:02:26 ON 03 NOV 2009
Copyright (c) 2009 The Thomson Corporation

FILE 'EMBASE' ENTERED AT 10:02:26 ON 03 NOV 2009
Copyright (c) 2009 Elsevier B.V. All rights reserved.

=> s (l1 or brassinin) and (cancer or tumor or tumour or neoplasm)
L2          81 (L1 OR BRASSININ) AND (CANCER OR TUMOR OR TUMOUR OR NEOPLASM)

=> s l2 and synerg?
L3           2 L2 AND SYNERG?

=> d l3 ibib abs 1-2

L3   ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:        2007:465345  CAPLUS
DOCUMENT NUMBER:         148:45359
TITLE:                   Effects of indole phytoalexins from cruciferous plants
                         on the growth of cancer cells. Implications
                         for cancer chemoprevention and chemotherapy
AUTHOR(S):               Mezencev, Roman; Mojzis, Jan; Pilatova, Martina;
                         Kutschy, Peter; Curillova, Zuzana
CORPORATE SOURCE:        United Nations, New York, NY, 10017, USA
SOURCE:                  International Journal of Cancer Prevention (2004),
                         1(2), 105-112
                         CODEN: IJCPC6; ISSN: 1554-1134
PUBLISHER:               Nova Science Publishers, Inc.
DOCUMENT TYPE:           Journal
LANGUAGE:                English
```

AB Cruciferous vegetables (Brassicaceae) possess epidemiol. and exptl. proven cancer chemopreventive activity. Indole phytoalexins, produced by these plants after their exposure to various forms of stress, have been recently shown to exhibit cancer chemopreventive activity (brassinin, cyclobrassinin, spirobrassinin) and/or direct antiproliferative activity (brassinin, spirobrassinin, brassilexin, camalexin) against various cancer cell lines in vitro. Our results suggest that in addition to their proven chemopreventive activity, brassinin surprisingly exhibits both antiproliferative (MDA-MB-231, U-87 MG) and growth-promoting (MCF-7, CACO-2) activity on cancer cells, while spirobrassinin consistently inhibited growth of all mentioned cell lines. However, according to QSAR prediction, spirobrassinin, unlike brassinin, is reasonably expected to be a mutagenic phytochem. Summarily, future role of both these indole phytoalexins in cancer chemoprevention is questionable. Significant potentiation of vincristine cytotoxicity to U-87 MG cells by brassinin, spirobrassinin, 1-methoxyspirobrassinin and 1-methoxyspirobrassinol, as well as drug-like character of these compds. suggest possibility of their future role in combination chemotherapy. Considering that small structural differences of indole phytoalexins result in great changes of their effects on cancer cells, there is need for further studies of indole phytoalexins focused on their effects on malignant tumors growth in vivo, mechanisms of their activity and structure-property (activity) relationships.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2006:899245 CAPLUS

DOCUMENT NUMBER: 145:448764

TITLE: Mechanism of Increased Coxsackie and Adenovirus Receptor Gene Expression and Adenovirus Uptake by Phytoestrogen and Histone Deacetylase Inhibitor in Human Bladder Cancer Cells and the Potential Clinical Application

AUTHOR(S): Pong, Rey-Chen; Roark, Ryan; Ou, Jiun-Yih; Fan, Jianhai; Stanfield, Jennifer; Frenkel, Eugene; Sagalowsky, Arthur; Hsieh, Jer-Tsong

CORPORATE SOURCE: Department of Urology, University of Texas Southwestern Medical Center, Dallas, TX, USA

SOURCE: Cancer Research (2006), 66(17), 8822-8828
CODEN: CNREA8; ISSN: 0008-5472

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Coxsackie and adenovirus receptor (CAR) is known as a principal receptor for adenovirus commonly used as a gene delivery vector. Down-regulation of CAR is often detected in several cancer types. Epigenetic modifiers such as histone deacetylase inhibitor FK228 (depsipeptide) have been shown to increase CAR expression as well as the uptake of adenovirus in bladder cancer in vivo and in vitro, indicating that altered transcriptional regulation of CAR is the key mechanism responsible for the decreased CAR levels in this cancer. In this study, we screened agents that could induce CAR expression in bladder cancer cells. Fifty-eight drugs with various chemical properties were tested. Ipriflavone and plant isoflavones were found to exhibit the ability to induce CAR gene expression in combination with FK228. Genistein, the natural isoflavone found in soybean, when combined with FK228, exerts a synergistic effect on CAR gene and protein expression in bladder cancer cells. Chromatin immunopptn. results showed an increased histone

acetylation in the CAR promoter gene, which is due to the suppression of histone deacetylase activity by both agents. Also, our data indicated that combination treatment is a potent chemotherapeutic regimen for bladder cancer cells and the subsequent administration of recombinant adenovirus could further eliminate the remaining cells. Taken together, our results provide a strong rationale for combining chemotherapeutic and gene therapeutic agents to enhance the therapeutic efficacy in bladder cancer.

OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s l2 and py<=2003
L4 43 L2 AND PY<=2003

=> dup rem l4
PROCESSING COMPLETED FOR L4
L5 22 DUP REM L4 (21 DUPLICATES REMOVED)

=> d l5 ibib abs 1-22

L5 ANSWER 1 OF 22 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2003:807352 CAPLUS
DOCUMENT NUMBER: 140:174215
TITLE: Antiproliferative and cancer chemopreventive activity of phytoalexins: focus on indole phytoalexins from crucifers
AUTHOR(S): Mezencev, R.; Mojzis, J.; Pilatova, M.; Kutschy, P.
CORPORATE SOURCE: Verification and Inspection Commission, United Nations Monitoring, New York, NY, 10017, USA
SOURCE: Neoplasma (2003), 50(4), 239-245
CODEN: NEOLA4; ISSN: 0028-2685
PUBLISHER: VEDA
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

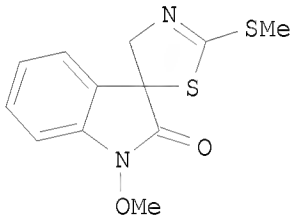
AB A review. Phytoalexins are produced by plants after exposure to phys., biol. or chemical stress and a specific group of these metabolites represent indole phytoalexins produced by important plants of the family Cruciferae. With respect to the epidemiol. proven cancer chemopreventive properties of brassica vegetables, antiproliferative and anticarcinogenic activities of indole phytoalexins have been studied. Several indole phytoalexins (i.e. brassinin, spirobrassinin, brassilexin, camalexin, 1-methoxyspirobrassinin, 1-methoxyspirobrassinol and methoxyspirobrassinol Me ether) have been found to possess significant antiproliferative activity against various cancer cells and this activity is supposed to be associated with the modulation of activity of transcription factors regulating cell cycle, differentiation and apoptosis. Indole phytoalexins (i.e. cyclobrassinin, spirobrassinin, brassinin) also exhibited cancer chemopreventive activity in models of mammary and skin carcinogenesis. Understanding the mol. and cellular mechanism of action of such drugs and their structure-activity relationships is necessary for development new derivs. with more favorable profile of antiproliferative and chemopreventive activities.

OS.CITING REF COUNT: 19 THERE ARE 19 CAPLUS RECORDS THAT CITE THIS RECORD (19 CITINGS)

REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2002:924930 CAPLUS
DOCUMENT NUMBER: 138:254987
TITLE: Spirocyclization strategy toward indole phytoalexins. The first synthesis of (±)-1-methoxyspirobrassinin, (±)-1-methoxyspirobrassinol, and (±)-1-methoxyspirobrassinol methyl ether
AUTHOR(S): Kutschy, Peter; Suchy, Mojmir; Monde, Kenji; Harada, Nobuyuki; Maruskova, Renata; Curillova, Zuzana; Dzurilla, Milan; Miklosova, Mariana; Mezencev, Roman; Mojzis, Jan
CORPORATE SOURCE: Faculty of Science, Institute of Chemical Sciences, P. J. Safarik University, Kosice, 041 67, Slovakia
SOURCE: Tetrahedron Letters (2002), 43(52), 9489-9492
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:254987
GI



I

AB The first syntheses of cruciferous indole phytoalexins (±)-1-methoxyspirobrassinin (I), (±)-1-methoxyspirobrassinol, (±)-1-methoxyspirobrassinol Me ether as well as a new syntheses of phytoalexins (±)-spirobrassinin and cyclobrassinin were achieved by dioxane dibromide (DDB)-mediated spirocyclization of brassinin and its 1-substituted derivs. (±)-1-Methoxyspirobrassinol Me ether inhibited the growth of CACO-2 cell line to 38%.

OS.CITING REF COUNT: 20 THERE ARE 20 CAPLUS RECORDS THAT CITE THIS RECORD (20 CITINGS)
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 22 MEDLINE on STN
ACCESSION NUMBER: 2002492977 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12354359
TITLE: Discovery of cancer preventive agents from natural products: from plants to prevention.
AUTHOR: Mehta Rajendra G; Pezzuto John M
CORPORATE SOURCE: Department of Medicinal Chemistry and Pharmacognosy (MC 877), College of Pharmacy, University of Illinois at Chicago, Chicago, IL 60612, USA.
CONTRACT NUMBER: P01 CA48112 (United States NCI NIH HHS)
SOURCE: Current oncology reports, (2002 Nov) Vol. 4, No. 6, pp. 478-86. Ref: 50
Journal code: 100888967. ISSN: 1523-3790.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 1 Oct 2002
Last Updated on STN: 12 Mar 2003
Entered Medline: 11 Mar 2003

AB Cancer chemoprevention has traditionally been defined as a dietary or therapeutic approach for the prevention, delay, or reversal of carcinogenesis. We currently expand this definition to include nontoxic applications for patients with established disease. In this context, efficacy can be achieved by selectively altering cell-cycle progression. In the quest for new cancer chemopreventive agents, we have focused on the isolation of natural products as lead molecules, followed by synthetic modification to improve activity. Using biologic response as a guide for fractionation, over 200 active compounds have been identified. Some of the most interesting include brassinin and 4'-bromoflavone as inducers of quinone reductase, deguelin as an inhibitor of ornithine decarboxylase, resveratrol as an inhibitor of cyclooxygenase, and brusatol as an inducer of cellular differentiation. These agents have demonstrated effectiveness in experimental models of carcinogenesis. Further development of these agents as chemopreventive drugs may proceed through the normal regulatory process (eg, 4'-bromoflavone). Alternatively, some natural products may be administered as dietary supplements (eg, resveratrol). In either case, chemoprevention offers great hope in reducing the morbidity and mortality associated with cancer.

L5 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2002:913009 CAPLUS
DOCUMENT NUMBER: 138:286565
TITLE: Botanicals in cancer chemoprevention
AUTHOR(S): Park, Eun-Jung; Pezzuto, John M.
CORPORATE SOURCE: College of Pharmacy, Department of Medicinal Chemistry and Pharmacognosy, Program for Collaborative Research in Pharmaceutical Sciences, University of Illinois, Chicago, IL, USA
SOURCE: Cancer and Metastasis Reviews (2002), 21(3-4), 231-255
CODEN: CMRED4; ISSN: 0167-7659
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Botanicals have been used for the treatment of various human diseases throughout history. In addition, botanicals play a role in disease prevention. For example, epidemiol. studies have suggested that a reduced risk of cancer is associated with high consumption of vegetables and fruits. Thus, the cancer chemopreventive potential of naturally occurring phytochems. is of great interest. In this review, we discuss the cancer chemopreventive activity of cruciferous vegetables such as cabbage and broccoli, Allium vegetables such as garlic and onion, green tea, Citrus fruits, tomatoes, berries, ginger and ginseng, as well as some medicinal plants. In addition, methods for the discovery of active compds. from plant sources are described. Several lead compds., such as brassinin (from cruciferous vegetables like Chinese cabbage), sulforaphane (from broccoli) and its analog sulforamate, withanolides (from tomatillos), and resveratrol (from grapes and peanuts among other foods), are in preclin. or clin. trials for cancer chemoprevention. Phytochems. of these types have great potential in the fight against human cancer, and a variety of delivery methods are available as a result of their occurrence in nature.

OS.CITING REF COUNT: 90 THERE ARE 90 CAPLUS RECORDS THAT CITE THIS RECORD (91 CITINGS)
REFERENCE COUNT: 183 THERE ARE 183 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 2002:467625 CAPLUS
DOCUMENT NUMBER: 137:357962
TITLE: Evaluation of selected chemopreventive agents present in common foods in mouse mammary gland organ culture
AUTHOR(S): Hawthorne, Michael; Steele, Vernon; Mehta, Rajendra G.
CORPORATE SOURCE: Department of Surgical Oncology, College of Medicine, University of Illinois at Chicago, Chicago, IL, 60612, USA
SOURCE: Pharmaceutical Biology (Lisse, Netherlands) (2002), 40(Suppl.), 70-74
CODEN: PHBIFC; ISSN: 1388-0209
PUBLISHER: Swets & Zeitlinger B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Prevention of cancer by natural and synthetic non-toxic chemopreventive agents has become a major research area in the past 15 yr. The naturally occurring chemopreventive agents from the herbal medicine and edible plants can be evaluated in a variety of bioassays and identified for their activity as cancer preventive agents. We have adapted a mouse mammary gland organ culture assay (MMOC) for evaluating CP chemopreventive agents for their activity to inhibit 7,12-dimethylbenz(a)anthracene (DMBA)-induced mammary alveolar lesions (MAL). Here, we report a list of 32 agents that are found in the herbs or edible foods and showing inhibition of more than 55% in MMOC. From the studies reported in the literature it appears that there is a good correlation between the effects in MMOC and effects observed with in vivo carcinogenesis models. Recently, we have modified the MMOC assay to evaluate efficacy of chemopreventive agents specifically the ones that may have anti-estrogenic activity. Thus, MMOC provides a valuable tool for preliminary evaluation of chemopreventive agents prior to conducting a long-term animal carcinogenesis studies.
OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 22 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2002223932 EMBASE
TITLE: Cruciferous vegetables and cancer prevention.
AUTHOR: Murillo, Genoveva; Mehta, Rajendra G., Dr. (correspondence)
CORPORATE SOURCE: Dept. of Surgical Oncology (MC/820), Univ. of Illinois Coll. of Medicine, Clinical Science Bldg., 840 S. Wood St., Chicago, IL 60612-7322, United States.
SOURCE: Nutrition and Cancer, (2001) Vol. 41, No. 1-2, pp. 17-28.
Refs: 103
ISSN: 0163-5581 CODEN: NUCADQ
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 016 Cancer
017 Public Health, Social Medicine and Epidemiology
029 Clinical and Experimental Biochemistry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 18 Jul 2002
Last Updated on STN: 18 Jul 2002

AB In recent years, cancer prevention by natural products has received considerable attention. The potential protective role of cruciferous vegetables and active components present in these vegetables, such as isothiocyanates and indole-3-carbinol, has been extensively studied in experimental in vitro and in vivo carcinogenesis models. Results have consistently shown that the chemopreventive agents derived from this class of vegetables of the Cruciferae family influence carcinogenesis during initiation and promotion phases of cancer development. Similarly, reports from epidemiological studies and clinical trials support this notion. However, there is no comprehensive summary of all these aspects of the association between cruciferous vegetables and cancer prevention. We have attempted to summarize experimental carcinogenesis studies as well as clinical trials and studies on the mechanism of action of selective chemopreventive agents isolated and identified within these natural products. Results clearly point toward a positive correlation between cancer prevention of many target organs and consumption of cruciferous vegetable or their active constituents. Yet we are still far from complete understanding of the effects of combinations of chemopreventive phytochemicals present in these cruciferous vegetables and their overall mechanism(s) of action in providing protective effects.

L5 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 5
ACCESSION NUMBER: 2001:116397 CAPLUS
DOCUMENT NUMBER: 135:116709
TITLE: Cytotoxic effect of cruciferous phytoalexins against murine L1210 leukemia and B16 melanoma
AUTHOR(S): Sabol, Marian; Kutschy, Peter; Siegfried, Leonard; Mirossay, Andrej; Suchy, Mojmir; Hrbkova, Helga; Dzurilla, Milan; Maruskova, Renata; Starkova, Julia; Paulikova, Edita
CORPORATE SOURCE: Institute of Medical Microbiology, Medical Faculty, P.J. Safarik University, Kosice, SK-04180, Slovakia
SOURCE: Biologia (Bratislava) (2000), 55(6), 701-707
CODEN: BLOAAO; ISSN: 0006-3088
PUBLISHER: Slovak Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cytotoxic effect of brassinin, spirobrassinin and cyclobrassinin was tested against mouse leukemia (L1210) and melanoma (B16) cell lines. The most active phytoalexin was brassinin. Concentration of 100 μM reduced the cell growth of murine leukemia L1210 and melanoma B16 cell lines by 35% of solvent control after 24h of cultivation. Spirobrassinin was less efficient against both cell lines and concentration of 100 μM inhibited cell growth by 13%. Cyclobrassinin has lower solubility and at tested concns. (10-0.1 μM) did not influence cell growth of L1210 or B16 cell lines. The attempt was made to investigate the chemosensitizing capacity of brassinin, but no sensitizing effect of brassinin to vincristine cytotoxicity against resistant L1210/VCR line was found. To the authors' best knowledge, this is the first report on the study of the cytotoxic effect of brassinin and spirobrassinin and chemosensitizing potential of brassinin against cancer cell lines.

OS.CITING REF COUNT: 22 THERE ARE 22 CAPLUS RECORDS THAT CITE THIS RECORD (22 CITINGS)
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 22 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 1997:232646 BIOSIS

DOCUMENT NUMBER: PREV199799531849
TITLE: Brassinin-mediated induction of phase II detoxification enzymes in rat liver and mammary glands.
AUTHOR(S): Gerhaeuser, C. [Reprint author]; Thomas, C. F.; Moon, R. C.; Pezzuto, J. M.
CORPORATE SOURCE: Deutsches Krebsforschungszentrum, 69120 Heidelberg, Germany
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (1997) Vol. 38, No. 0, pp. 365.
Meeting Info.: Eighty-eighth Annual Meeting of the American Association for Cancer Research. San Diego, California, USA. April 12-16, 1997.
ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 2 Jun 1997
Last Updated on STN: 2 Jun 1997

L5 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 6
ACCESSION NUMBER: 1997:71620 CAPLUS
DOCUMENT NUMBER: 126:180907
ORIGINAL REFERENCE NO.: 126:34761a,34764a
TITLE: Cancer chemopreventive potential of sulforamate, a novel analog of sulforaphane that induces phase 2 drug-metabolizing enzymes
AUTHOR(S): Gerhauser, Clarissa; You, Min; Liu, Jinfang; Moriarty, Robert M.; Hawthorne, Michael; Mehta, Rajendra G.; Moon, Richard C.; Pezzuto, John M.
CORPORATE SOURCE: Department of Medicinal Chemistry and Pharmacognosy, College of Pharmacy, University of Illinois at Chicago, Chicago, IL, 60612, USA
SOURCE: Cancer Research (1997), 57(2), 272-278
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Chemoprevention involves the use of natural or synthetic substances to reduce the risk of developing cancer. Two dietary components capable of mediating chemopreventive activity in animal models by modulation of drug-metabolizing enzymes are sulforaphane, an aliphatic isothiocyanate, and brassinin, an indole-based dithiocarbamate, both found in cruciferous vegetables. The authors currently report the synthesis and activity of a novel cancer chemopreventive agent, (±)-4-methylsulfinyl-1-(S-methyldithiocarbamyl)-butane (trivial name, sulforamate), an aliphatic analog of brassinin with structural similarities to sulforaphane. This compound was shown to be a monofunctional inducer of NAD(P)H:quinone oxidoreductase [quinone reductase (QR)], a Phase II enzyme, in murine Hepa 1c1c7 cell culture and two mutants thereof. Induction potential was comparable to that observed with sulforaphane (concentration required to double the specific activity of QR, .apprx.0.2 μM), but cytotoxicity was reduced by about 3-fold (IC50 .apprx.30 μm). In addition, sulforaphane, as well as the analog, increased glutathione levels about 2-fold in cultured Hepa 1c1c7 cells. Induction of QR was regulated at the transcriptional level. Using Northern blotting techniques, time- and dose-dependent induction of QR mRNA levels were demonstrated in Hepa 1c1c7 cell culture. To further investigate the mechanism of induction, HepG2 human hepatoma cells were transiently transfected with QR-chloramphenicol acetyltransferase plasmid constructs containing various portions of the 5'-region of the QR gene. Sulforaphane and the analog significantly induced CAT activity at a concentration

of 12.5 μM by interaction with the antioxidant responsive element (5-14-fold induction) without interacting with the xenobiotic responsive element. Moreover, both compds. significantly induced mouse mammary QR and glutathione S-transferase activity (feeding of 3 mg/mouse intragastric for 4 days), whereas the elevation of hepatic enzyme activities was less pronounced. Both sulforaphane and the analog were identified as potent inhibitors of preneoplastic lesion formation in carcinogen-treated mouse mammary glands in organ culture (84% and 78% inhibition at 1 μm, resp.). On the basis of these results, the sulforaphane analog can be regarded as a readily available promising new cancer chemopreventive agent.

OS.CITING REF COUNT: 154 THERE ARE 154 CAPLUS RECORDS THAT CITE THIS RECORD (155 CITINGS)

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 10 OF 22 EMBASE

ACCESSION NUMBER: 1997128182 EMBASE

TITLE: Assessment of antimutagenic activity with Salmonella typhimurium strain TM677.

AUTHOR: Shamon, Lisa A.; Pezzuto, John M., Dr. (correspondence)
CORPORATE SOURCE: Prog. Collab. Res. Pharmaceut. Sci., College of Pharmacy, University of Illinois at Chicago, IL, United States. jpezzuto@uic.edu
AUTHOR: Pezzuto, John M., Dr. (correspondence)
CORPORATE SOURCE: Prog. Collab. Res. Pharmaceut. Sci., Department of Medicinal Chemistry, University of Illinois at Chicago, 833 S. Wood Street, Chicago, IL 60612, United States. jpezzuto@uic.edu
AUTHOR: Pezzuto, John M., Dr. (correspondence)
CORPORATE SOURCE: Program Collab. Research Pharm. Sci., Dept. Medicinal Chem. Pharmacognosy, University of Illinois at Chicago, 833 S Wood Street, Chicago, IL 60612, United States. jpezzuto@uic.edu

SOURCE: Methods in Cell Science, (1997) Vol. 19, No. 1, pp. 57-62. Refs: 21
ISSN: 1381-5741 CODEN: MCSCFB
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
029 Clinical and Experimental Biochemistry
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 29 May 1997
Last Updated on STN: 29 May 1997

AB A method is described for the detection of antimutagenic agents in a forward mutation assay with Salmonella typhimurium strain TM677. Bacterial cells are treated with test compounds in the presence of a known mutagen. Antimutagenic activity is indicated by a reduction in the induced mutant fraction. This assay has been used to detect and/or confirm the antimutagenic activity of a number of known compounds. This method is currently being used in our laboratory for the bioassay-directed fractionation of potential cancer chemoprevention agents from plant extracts.

L5 ANSWER 11 OF 22 CAPLUS DUPLICATE 7

ACCESSION NUMBER: 1998:10422 CAPLUS

DOCUMENT NUMBER: 128:124721
ORIGINAL REFERENCE NO.: 128:24371a,24374a
TITLE: Role of the estrogen receptor in the action of organochlorine pesticides on estrogen metabolism in human breast cancer cell lines
AUTHOR(S): Leon Bradlow, H.; Davis, Devra; Sepkovic, Daniel W.; Tiwari, Raj; Osborne, Michael P.
CORPORATE SOURCE: Strang Cancer Research Laboratory, New York, USA
SOURCE: Science of the Total Environment (1997), 208(1,2), 9-14
CODEN: STENDL; ISSN: 0048-9697
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB As interest in the properties of xenoestrogenic compds. has grown, different in vitro cell culture systems have been proposed as models, against which to gauge relative estrogenic impact. Previous research indicated that some organochlorine-based pesticides elevated the production of 16α-hydroxyestrone relative to 2-hydroxyestrone in ER+ MCF-7 breast cancer cells while phytochems. like indole-3-carbinol reduced this ratio. That this ratio may be a biol. marker of the risk of breast cancer has recently been demonstrated. In this study the authors have carried out the same paradigm in two ER- cell lines to examine the effect of receptor status. To determine whether the impact of chlorinated pesticides can be modulated by phytochems., the ability of indole-3-carbinol or brassinin to reverse the changes in metabolism was examined Non-persisting phosphorus-based pesticides were also studied and shown not to have an effect on estrogen metabolism The implications of these findings are examined
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 12 OF 22 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 1996:255932 BIOSIS
DOCUMENT NUMBER: PREV199698812061
TITLE: Effect of terpenes and differentiation inducers on ornithine decarboxylase (ODC) activity: A specific in vitro assay model for screening of potential chemopreventive agents.
AUTHOR(S): Desai-Reddy, N. [Reprint author]; Sharma, S. [Reprint author]; Kelloff, G. J. [Reprint author]; Steele, V. E.
CORPORATE SOURCE: ManTech Environ. Technol. Inc., Research Triangle Park, NC 27709, USA
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (1996) Vol. 37, No. 0, pp. 268.
Meeting Info.: 87th Annual Meeting of the American Association for Cancer Research. Washington, D.C., USA. April 20-24, 1996.
ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 31 May 1996
Last Updated on STN: 11 Jul 1996

L5 ANSWER 13 OF 22 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 1995:187698 BIOSIS
DOCUMENT NUMBER: PREV199598201998
TITLE: Transcriptional regulation of drug metabolizing enzymes by

brassinin and derivatives.
AUTHOR(S): Gerhauser, C. [Reprint author]; You, M.; Liu, J.; Moriarty, R. M.; Rundhaugen, L. M.; Barch, D. H.; Pezzuto, J. M.
CORPORATE SOURCE: Coll. Pharm. Liberal Arts Sci., Univ. Ill. at Chicago, Chicago, IL, USA
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (1995) Vol. 36, No. 0, pp. 590.
Meeting Info.: Eighty-sixth Annual Meeting of the American Association for Cancer Research. Toronto, Ontario, Canada. March 18-22, 1995.
ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 5 May 1995
Last Updated on STN: 9 Jun 1995

L5 ANSWER 14 OF 22 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 8
ACCESSION NUMBER: 1995:464981 CAPLUS
DOCUMENT NUMBER: 122:230157
ORIGINAL REFERENCE NO.: 122:41755a,41758a
TITLE: Cancer-chemopreventive activity of brassinine, a phytoalexin from cabbage
AUTHOR(S): Mehta, Rajendra G.; Liu, Jinfang; Constantinou, Andreas; Thomas, Cathy F.; Hawthorne, Michael; You, Min; Gerhaeuser, Clarissa; Pezzuto, John M.; Moon, Richard C.; Moriarty, Robert M.
CORPORATE SOURCE: College Medicine, Univ. Illinois, Chicago, IL, 60612, USA
SOURCE: Carcinogenesis (1995), 16(2), 399-404
CODEN: CRNGDP; ISSN: 0143-3334
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Brassinine [3-(S-methyldithiocarbamoyl)aminomethylindole], a phytoalexin first identified as a constituent of cabbage, was synthesized and evaluated for cancer-chemopreventive activity. Dose-dependent inhibition of 7,12-dimethylbenz[a]anthracene (DMBA)-induced preneoplastic lesion formation was observed with mouse mammary glands in organ culture, as was dose-dependent inhibition of DMBA-induced mouse skin tumors that were promoted by treatment with 12-O-tetradecanoylphorbol-13-acetate. Cyclobrassinine is a biol. derived product of the oxidative cyclization of brassinine, and was as active as the parent compound in inhibiting the formation of preneoplastic mammary lesions in culture; however, 2-methylbrassinine was not active in this process. Therefore, oxidative cyclization may be an effective metabolic activation step. As judged by these tumor inhibition studies in conjunction with potential to induce phase II enzymes in mice or cell culture, brassinine may be effective as a chemopreventive agent during both the initiation and promotion phases of carcinogenesis. This is the 1st report documenting the chemopreventive potential of structurally novel indole-based phytoalexins that are naturally occurring in cruciferous vegetables, and the synthetic route described herein has proven amenable for scale-up production The bifunctional structural nature of brassinine, bearing both an indole nucleus and a dithiocarbamoylaminomethyl moiety, is notably similar to the individual structural elements of other known chemopreventive agents such as indole-3-carbinol or benzylisothiocyanate. The favorable biol. activity demonstrated by the compound may originate from the presence of these 2 moieties.
OS.CITING REF COUNT: 96 THERE ARE 96 CAPLUS RECORDS THAT CITE THIS RECORD (97 CITINGS)

L5 ANSWER 15 OF 22 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1995:924890 CAPLUS
TITLE: Oxidative cyclization of brassinin and homobrassinin
AUTHOR(S): Moriarty, Robert M.; Liu, Jinfang
CORPORATE SOURCE: Department Chemistry, University Illinois, Chicago, IL, 60607-7061, USA
SOURCE: Book of Abstracts, 210th ACS National Meeting, Chicago, IL, August 20-24 (1995), Issue Pt. 2, ORGN-276. American Chemical Society: Washington, D. C.
CODEN: 61XGAC
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB Brassinin, an antimicrobial and cancer chemopreventive agent was oxidatively cyclized under various condition to spirobrassinin, cyclobrassinin and spiro compound Results with the higher homolog, homobrassinin, under oxidative cyclization conditions will also be reported.

L5 ANSWER 16 OF 22 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 1995:422842 BIOSIS
DOCUMENT NUMBER: PREV199598437142
TITLE: Oxidative cyclization of brassinin and homobrassinin.
AUTHOR(S): Moriarty, Robert M.; Liu, Jinfang
CORPORATE SOURCE: Dep. Chem., Univ. Ill. Chicago, Chicago, IL 60607-7061, USA
SOURCE: Abstracts of Papers American Chemical Society, (1995) Vol. 210, No. 1-2, pp. ORGN 276.
Meeting Info.: 210th American Chemical Society National Meeting. Chicago, Illinois, USA. August 20-24, 1995.
CODEN: ACSRAL. ISSN: 0065-7727.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 3 Oct 1995
Last Updated on STN: 1 Nov 1995

L5 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 9
ACCESSION NUMBER: 1995:179429 CAPLUS
DOCUMENT NUMBER: 122:310
ORIGINAL REFERENCE NO.: 122:59a,62a
TITLE: Structure-activity relationships of brassinin in preventing the development of carcinogen-induced mammary lesions in organ culture
AUTHOR(S): Mehta, Rajendra G.; Liu, Jinfang; Constantinou, Andreas; Hawthorne, Michael; Pezzuto, John M.; Moon, Richard C.; Moriarty, Robert M.
CORPORATE SOURCE: College Medicine, University Illinois Chicago, Chicago, IL, 60612, USA
SOURCE: Anticancer Research (1994), 14(3A), 1209-13
CODEN: ANTRD4; ISSN: 0250-7005
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Brassinin, a phytoalexin, is found in Chinese cabbage. Previously, the authors showed that brassinin significantly inhibited dimethylbenz(a)anthracene (DMBA)-induced mammary lesions in organ culture. Moreover, it was an effective inhibitor against two stage skin carcinogenesis. In the present study, the authors synthesized several analogs of brassinin and evaluated their effectiveness in the mouse mammary gland organ culture model. Results showed that

cyclobrassinin, also a naturally occurring brassinin analog, was more effective than brassinin. Spirobrassinin and N-ethyl-2,3-dihydrobrassinin also significantly inhibited mammary lesion formation. However, none of the Me substituted analogs were effective. The effects of brassinin may, in part, be mediated by induction of phase II detoxifying enzymes such as quinone reductase.
OS.CITING REF COUNT: 49 THERE ARE 49 CAPLUS RECORDS THAT CITE THIS RECORD (52 CITINGS)

L5 ANSWER 18 OF 22 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 1994:291740 BIOSIS
DOCUMENT NUMBER: PREV199497304740
TITLE: Induction of quinone reductase activity mediated by brassinin and its derivatives.
AUTHOR(S): You, M. [Reprint author]; Gerhauser, C.; Liu, J.; Moriarty, R. M.; Metha, R. G.; Moon, R. C.; Pezzuto, J. M.
CORPORATE SOURCE: Coll. Liberal Arts Sci., Univ. Illinois at Chicago, Chicago, IL 60612, USA
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (1994) Vol. 35, No. 0, pp. 627.
Meeting Info.: 85th Annual Meeting of the American Association for Cancer Research. San Francisco, California, USA. April 10-13, 1994.
ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 30 Jun 1994
Last Updated on STN: 18 Nov 1994

L5 ANSWER 19 OF 22 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 1993:401193 BIOSIS
DOCUMENT NUMBER: PREV199345060018
TITLE: Identification and characterization of natural inhibitors of carcinogenesis.
AUTHOR(S): Beecher, C. W. W. [Reprint author]; Farnsworth, N. R.; Fong, H. H. S.; Kinghorn, A. D.; Mehta, R. G.; Moon, R. C.; Moriarty, R. M.; Pezzuto, J. M.; Soejarto, D. D.
CORPORATE SOURCE: Univ. Illinois Chicago, Chicago, IL, USA
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (1993) Vol. 34, No. 0, pp. 559.
Meeting Info.: 84th Annual Meeting of the American Association for Cancer Research. Orlando, Florida, USA. May 19-22, 1993.
ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting)
LANGUAGE: English
ENTRY DATE: Entered STN: 30 Aug 1993
Last Updated on STN: 3 Jan 1995

L5 ANSWER 20 OF 22 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 1993:359498 BIOSIS
DOCUMENT NUMBER: PREV199345042923
TITLE: Brassinin: A novel chemopreventive agent.
AUTHOR(S): Mehta, R. G.; Constantinou, A.; Moriarty, R.; Pezzuto, J. M.; Moon, R. C.
CORPORATE SOURCE: Specialized Cancer Cent., Univ. Ill., Chicago, IL 60612, USA
SOURCE: Proceedings of the American Association for Cancer Research

Annual Meeting, (1993) Vol. 34, No. 0, pp. 127.
Meeting Info.: 84th Annual Meeting of the American Association for Cancer Research. Orlando, Florida, USA. May 19-22, 1993.
ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting)
LANGUAGE: English
ENTRY DATE: Entered STN: 31 Jul 1993
Last Updated on STN: 31 Aug 1993

L5 ANSWER 21 OF 22 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 10
ACCESSION NUMBER: 1991:622929 CAPLUS
DOCUMENT NUMBER: 115:222929
ORIGINAL REFERENCE NO.: 115:37759a,37762a
TITLE: Growth inhibitions on human cancer cell cultures with the indole sulfur-containing phytoalexins and their analogs
AUTHOR(S): Tempete, Christiane; Devys, Michel; Barbier, Michel
CORPORATE SOURCE: Inst. Chim. Subst. Nat., CNRS, Gif sur Yvette, 91198, Fr.
SOURCE: Zeitschrift fuer Naturforschung, C: Journal of Biosciences (1991), 46(7-8), 706-7
CODEN: ZNCBDA; ISSN: 0341-0382
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cell growth inhibitions on human cancer cell cultures were determined for the indole sulfur-containing phytoalexins cyclobrassinin, brassilexin (previously isolated from vegetables of the Cruciferae family) and their synthetic analogs 5-methoxybrassilexin and homocyclobrassinin. The most biol. active of these products is brassilexin (LD50 = 8 μg/mL).
OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

L5 ANSWER 22 OF 22 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
ACCESSION NUMBER: 1991:52572 BIOSIS
DOCUMENT NUMBER: PREV199191030853; BA91:30853
TITLE: THE FIRST TOTAL SYNTHESES OF 9 METHOXYCARBAZOLE-3-CARBOXALDEHYDE AND METHOXYBRASSININ THE CHEMISTRY OF 1 METHOXYINDOLE.
AUTHOR(S): KAWASAKI T [Reprint author]; SOMEI M
CORPORATE SOURCE: FAC PHARM SCIENCES, KANAZAWA UNIVERSITY, 13-1 TAKARA-MACHI, KANAZAWA 920, JPN
SOURCE: Heterocycles (Tokyo), (1990) Vol. 31, No. 9, pp. 1605-1608.
CODEN: HTCYAM. ISSN: 0385-5414.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 10 Jan 1991
Last Updated on STN: 7 Mar 1991
AB The first total syntheses of an alkaloid 9-methoxycarbazole-3-carboxaldehyde and a phytoalexin methoxybrassinin are reported.

=>
Connecting via Winsock to STN

```
Welcome to STN International!  Enter x:X

LOGINID:ssptacrs1614

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1          Web Page for STN Seminar Schedule - N. America
 NEWS  2  JAN 12  Match STN Content and Features to Your Information
                  Needs, Quickly and Conveniently
 NEWS  3  JAN 25  Annual Reload of MEDLINE database
 NEWS  4  FEB 16  STN Express Maintenance Release, Version 8.4.2, Is
                  Now Available for Download
 NEWS  5  FEB 16  Derwent World Patents Index (DWPI) Revises Indexing
                  of Author Abstracts
 NEWS  6  FEB 16  New FASTA Display Formats Added to USGENE and PCTGEN
 NEWS  7  FEB 16  INPADOCDB and INPAFAMDB Enriched with New Content
                  and Features
 NEWS  8  FEB 16  INSPEC Adding Its Own IPC codes and Author's E-mail
                  Addresses
 NEWS  9  APR 02  CAS Registry Number Crossover Limits Increased to
                  500,000 in Key STN Databases
 NEWS 10  APR 02  PATDPAFULL: Application and priority number formats
                  enhanced
 NEWS 11  APR 02  DWPI: New display format ALLSTR available
 NEWS 12  APR 02  New Thesaurus Added to Derwent Databases for Smooth
                  Sailing through U.S. Patent Codes
 NEWS 13  APR 02  EMBASE Adds Unique Records from MEDLINE, Expanding
                  Coverage back to 1948
 NEWS 14  APR 07  CA/CAplus CLASS Display Streamlined with Removal of
                  Pre-IPC 8 Data Fields
 NEWS 15  APR 07  50,000 World Traditional Medicine (WTM) Patents Now
                  Available in CAplus
 NEWS 16  APR 07  MEDLINE Coverage Is Extended Back to 1947

 NEWS EXPRESS FEBRUARY 15 10 CURRENT WINDOWS VERSION IS V8.4.2,
              AND CURRENT DISCOVER FILE IS DATED 15 JANUARY 2010.

 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS LOGIN    Welcome Banner and News Items

Enter NEWS followed by the item number or name to see news on that
specific topic.

  All use of STN is subject to the provisions of the STN customer
  agreement.  This agreement limits use to scientific research.  Use
  for software development or design, implementation of commercial
  gateways, or use of CAS and STN data in the building of commercial
  products is prohibited and may result in loss of user privileges
  and other penalties.

* * * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 10:46:45 ON 27 MAY 2010

=> file caplus medline
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.22       0.22
```

```
FILE 'CAPLUS' ENTERED AT 10:47:09 ON 27 MAY 2010
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2010 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'MEDLINE' ENTERED AT 10:47:09 ON 27 MAY 2010

=> s indoleamine (s) inhibi?
L1         785 INDOLEAMINE (S) INHIBI?

=> s indoleamine? (s) inhibi?
L2         795 INDOLEAMINE? (S) INHIBI?

=> s l2 and (cancer or tumor or neoplasm)
L3         246 L2 AND (CANCER OR TUMOR OR NEOPLASM)

=> s l3 and cisplatin
L4           9 L3 AND CISPLATIN

=> dup rem l4
PROCESSING COMPLETED FOR L4
L5           8 DUP REM L4 (1 DUPLICATE REMOVED)

=> d l5 ibib abs 1-8

L5   ANSWER 1 OF 8  CAPLUS  COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER:        2009:617321  CAPLUS
DOCUMENT NUMBER:         150:555912
TITLE:                   3-Hydroxyanthranilic acid or salts thereof for
                         treating cancer or infections
INVENTOR(S):             Schofield, Christopher Joseph; Cerundolo, Vincenzo
PATENT ASSIGNEE(S):      Ludwig Institut fur Krebsforschung A.-G., USA; The
                         Chanceller, Masters and Scholars of the University of
                         Oxford
SOURCE:                  PCT Int. Appl., 39pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.         DATE
     ---------------     ----   --------    --------------------    --------
     WO 2009063241        A1    20090522    WO 2008-GB51059         20081113
         W:  AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ,
             CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES,
             FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE,
             KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD,
             ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH,
             PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ,
             TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU,
             IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK,
             TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD,
             TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW,
             AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
PRIORITY APPLN. INFO.:                       GB 2007-22274       A  20071113
AB   The invention discloses a novel inhibitor of indoleamine
     2,3-dioxygenase and its use in the treatment of cancer or
     infections, either alone or in combination with addnl. therapeutic agents.
OS.CITING REF COUNT:     1     THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD
```

(1 CITINGS)
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2010 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2009:1026321 CAPLUS
DOCUMENT NUMBER: 152:303609
TITLE: Indoleamine 2,3-dioxygenase as a new target for malignant glioma therapy
AUTHOR(S): Miyazaki, Takeshi; Moritake, Kouzo; Yamada, Kazuo; Hara, Nobumasa; Osago, Harumi; Shibata, Tomoko; Akiyama, Yasuhiko; Tsuchiya, Mikako
CORPORATE SOURCE: Department of Neurosurgery, Faculty of Medicine, Shimane University, Izumo, Shimane, Japan
SOURCE: Journal of Neurosurgery (2009), 111(2), 230-237
CODEN: JONSAC; ISSN: 0022-3085
PUBLISHER: American Association of Neurological Surgeons
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Object: Indoleamine 2,3-dioxygenase (IDO), a kynurenine pathway (KP) enzyme catalyzing oxidation of the essential amino acid tryptophan (Trp), is thought to be involved in the immune resistance of malignant tumors through T-cell inactivation caused by Trp depletion and metabolite accumulation. Human malignant gliomas may use this strategy to escape immune attack. The object of this study was to investigate the possibility of IDO-dependent Trp depletion by malignant gliomas and the practicability of using an IDO inhibitor together with anticancer drugs to reserve Trp without decreasing the cytotoxicity of the drugs. Methods: The authors studied expression of IDO and other KP enzymes and the effects of an IDO inhibitor, 1-Me L-tryptophan (1MT), on Trp metabolism and cytotoxicity of anticancer drugs, together with direct measurement of KP metabolites, in cultured human malignant glioma cells. Results: Upon interferon-γ (IFN-γ) stimulation, the glioma cells greatly increased their IDO mRNA expression concomitant with depletion of Trp. The IDO inhibitor 1MT successfully prevented Trp consumption by the stimulated glioma cells. Combining 1MT with anticancer drugs (temozolomide, bischloroethylnitrosourea [BCNU], etoposide and cisplatin) did not interfere with the drugs' suppression of growth of LN229 glioma cells but rather increased their inhibitory effects on IDO activity. Conclusions: These findings suggest that the robust IDO expression with rapid consumption of Trp in human glioma cells induced by IFN-γ could lead to immune resistance in glioma cells. Indoleamine 2,3-dioxygenase inhibitors that prevent Trp depletion could be used with anticancer drugs to improve therapeutic effects.
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2008:1156388 CAPLUS
DOCUMENT NUMBER: 149:402198
TITLE: Preparation of benzochromenedione derivatives for use as IDO inhibitors
INVENTOR(S): Prendergast, George C.; Malachowski, William P.; Muller, Alexander J.
PATENT ASSIGNEE(S): Lankenau Institute for Medical Research, USA
SOURCE: PCT Int. Appl., 46pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008115804	A1	20080925	WO 2008-US57032	20080314
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 2137168	A1	20091230	EP 2008-732234	20080314
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR				
US 20100076066	A1	20100325	US 2009-528466	20091203
PRIORITY APPLN. INFO.:			US 2007-918516P P	20070316
			WO 2008-US57032 W	20080314

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 149:402198
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I, II, and III [each R1 independently = H, halo, OH, etc.; each R2 = H or OH], and their pharmaceutically acceptable salts, are prepared and disclosed as indoleamine 2,3-dioxygenase (IDO) inhibitors. Thus, e.g., IV was prepared by cyclization of 2-hydroxy-1,4-naphthoquinone with 3-methyl-2-butenal. I, II, and III were evaluated in IDO inhibitory activity assays, e.g., IV demonstrated IC50 value of 0.155 μM.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2007:485452 CAPLUS
DOCUMENT NUMBER: 146:481923
TITLE: Dithiocarbamates as IDO inhibitors and their preparation, pharmaceutical compositions and their use in the treatment of diseases
INVENTOR(S): Duhadaway, James B.; Prendergast, George C.; Malachowski, William P.; Muller, Alexander J.
PATENT ASSIGNEE(S): Lankenau Institute for Medical Research, USA
SOURCE: PCT Int. Appl., 65pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007050963	A1	20070503	WO 2006-US42137	20061027
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,				

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN,
KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK,
MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO,
RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT,
TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM

US 20070105907	A1	20070510	US 2006-589024	20061027
US 7705022	B2	20100427		
EP 1940787	A1	20080709	EP 2006-844228	20061027

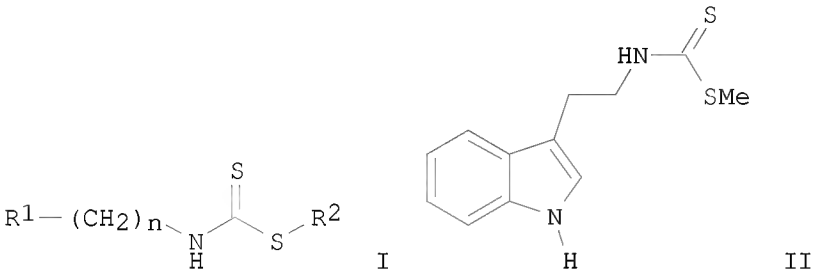
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR

PRIORITY APPLN. INFO.: US 2005-730706P P 20051027
WO 2006-US42137 W 20061027

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OTHER SOURCE(S): CASREACT 146:481923; MARPAT 146:481923

GI



I II

AB Dithiocarbamates of formula I as indoleamine 2,3-dioxygenase (IDO) inhibitors, compns. comprising the same, and methods of use thereof are disclosed. Compds. of formula I wherein R1 is cycloalkyl, aryl, indol-3-yl, benzofuran-3-yl, and benzothien-3-yl; R2 is alkenyl, Me, and CH2-aryl; n is 0 to 3; are claimed. Example compound II was prepared by dithiocarboxylation of tryptamine with carbon disulfide followed by methylation with Me iodide. All the invention compds. were evaluated for their IDO inhibitory activity. Example compound II exhibited Ki value of 82.54 μM.

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER:	2004:927197 CAPLUS
DOCUMENT NUMBER:	141:388648
TITLE:	Novel ido (indoleamine 2,3-dioxygenase) inhibitors and methods of use
INVENTOR(S):	Prendergast, George C.; Muller, Alexander J.; Duhadaway, James B.; Malachowski, William
PATENT ASSIGNEE(S):	Lankenau Institute for Medical Research, USA
SOURCE:	PCT Int. Appl., 115 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English

FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004094409	A1	20041104	WO 2004-US5154	20040220
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2520586	A1	20041104	CA 2004-2520586	20040220
EP 1606285	A1	20051221	EP 2004-713430	20040220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1795187	A	20060628	CN 2004-80008331	20040220
CN 1794986	A	20060628	CN 2004-80014321	20040220
JP 2006521377	T	20060921	JP 2006-508788	20040220
CN 101265254	A	20080917	CN 2008-10092243	20040220
CN 101265259	A	20080917	CN 2008-10092244	20040220
US 20070173524	A1	20070726	US 2006-550444	20060601
US 7714139	B2	20100511		
PRIORITY APPLN. INFO.:			US 2003-458162P P	20030327
			US 2003-527449P P	20031205
			CN 2004-80008331 A3	20040220
			WO 2004-US5154 W	20040220

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OTHER SOURCE(S): MARPAT 141:388648
AB Novel inhibitors of indoleamine 2,3-dioxygenase (IDO) activity are provided. In yet another embodiment of the present invention, a combination treatment protocol comprising administration of an IDO inhibitor with a signal transduction inhibitor (STI) or chemotherapeutic agent is provided, which is effective for suppressing tumor growth. In still another embodiment of the present invention, a combination treatment protocol is provided for the treatment of a chronic viral infection, comprising the administration of an IDO inhibitor and a chemotherapeutic agent.
OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2010 ACS on STN
ACCESSION NUMBER: 2004:927043 CAPLUS
DOCUMENT NUMBER: 141:388646
TITLE: Novel methods for the treatment of cancer and viral infections
INVENTOR(S): Prendergast, George C.; Muller, Alexander J.; Duhadaway, James B.; Malachowski, William
PATENT ASSIGNEE(S): Lankenau Institute for Medical Research, USA
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004093871	A1	20041104	WO 2004-US5155	20040220
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2520172	A1	20041104	CA 2004-2520172	20040220
EP 1613308	A1	20060111	EP 2004-713378	20040220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1795187	A	20060628	CN 2004-80008331	20040220
CN 1794986	A	20060628	CN 2004-80014321	20040220
JP 2006521378	T	20060921	JP 2006-508789	20040220
CN 101265254	A	20080917	CN 2008-10092243	20040220
CN 101265259	A	20080917	CN 2008-10092244	20040220
US 20070099844	A1	20070503	US 2006-551151	20060518
PRIORITY APPLN. INFO.:			US 2003-458162P P	20030327
			US 2003-527449P P	20031205
			CN 2004-80008331 A3	20040220
			WO 2004-US5155 W	20040220

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB Compns. and methods for the treatment of malignancy and chronic viral infection are disclosed. A method is claimed for treating a cancer comprising administering at least one indoleamine 2,3-dioxygenase (IDO) inhibitor and at least one signal transduction inhibitor (STI). A method is claimed for treating a cancer comprising administering at least one immunomodulator, other than IDO inhibitor, and at least one cytotoxic chemotherapeutic agent or at least one STI. A method for treating a chronic viral infection in a patient is claimed comprising administering at least one IDO inhibitor and at least one chemotherapeutic agent. Pharmaceutical compns. containing compds. of the invention for treating cancer and viral infections are also claimed.

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2004:1019533 CAPLUS

DOCUMENT NUMBER: 141:420433

TITLE: Use of inhibitors of indoleamine -2,3-dioxygenase in combination with other therapeutic modalities in the treatment of cancer and infection

INVENTOR(S): Munn, David; Mellor, Andrew

PATENT ASSIGNEE(S): Medical College of Georgia Research Institute, Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 42 pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 20040234623	A1	20041125	US 2004-780797		20040217
US 7598287	B2	20091006			
US 20050186289	A1	20050825	US 2004-780150		20040217
US 20090081155	A1	20090326	US 2008-175538		20080718
US 20090123420	A1	20090514	US 2008-175518		20080718
PRIORITY APPLN. INFO.:			US 2003-459489P	P	20030401
			US 2004-538647P	P	20040122
			US 2004-780150	A1	20040217
			US 2004-780797	A1	20040217

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention discloses a method for treating a subject with a cancer or an infection, the method including administering an inhibitor of indoleamine-2,3-dioxygenase (IDO) in an amount effective to reverse IDO-mediated immunosuppression, and administering at least one addnl. therapeutic agent, wherein the administration of the inhibitor of IDO and the at least one addnl. therapeutic agent demonstrate therapeutic synergy.

OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)

REFERENCE COUNT: 387 THERE ARE 387 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2010 ACS on STN

ACCESSION NUMBER: 2005:385509 CAPLUS

DOCUMENT NUMBER: 142:409490

TITLE: rIFN-γ-mediated growth suppression of platinum-sensitive and -resistant ovarian tumor cell lines not dependent upon arginase inhibition

AUTHOR(S): Melichar, Bohuslav; Hu, Wei; Patenia, Rebecca; Melicharova, Karolina; Gallardo, Stacie T.; Freedman, Ralph

CORPORATE SOURCE: Department of Oncology and Radiotherapy, Charles University Medical School, Hradec Kralove, Czech Rep.

SOURCE: Journal of Translational Medicine (2003), 1, No pp. given
CODEN: JTMOBV; ISSN: 1479-5876
URL: http://www.translational-medicine.com/content/pdf/1479-5876-1-5.pdf

PUBLISHER: BioMed Central Ltd.

DOCUMENT TYPE: Journal; (online computer file)

LANGUAGE: English

AB Arginine metabolism in tumor cell lines can be influenced by various cytokines, including recombinant human interferon-γ (rIFN-γ), a cytokine that shows promising clin. activity in epithelial ovarian cancer (EOC). Here, the authors examined EOC cell lines for the expression of arginase in an enzymic assay and for transcripts of arginase I and II, inducible nitric oxide synthase (iNOS), and indoleamine 2,3-dioxygenase (IDO) by reverse transcription-polymerase chain reaction. The effects of rIFNγ on arginase activity and on tumor cell growth inhibition were determined by measuring [3H]thymidine uptake. Elevated arginase activity was detected in 5 of 8 tumor cell lines, and anal. at the transcriptional level showed that arginase II was involved but arginase I was not. RIFN-γ reduced arginase activity in 3 EOC cell lines but increased activity in the 2008 cell line and its platinum-resistant subline, 2008.C13. INOS transcripts were not detected in rIFN-γ-treated or untreated cell lines. In contrast, IDO activity was induced or increased by rIFN-γ. Suppression of arginase activity by rIFN-γ in certain cell lines suggested that

such inhibition might contribute to its antiproliferative effects. However, supplementation of the medium with polyamine pathway products did not interfere with the growth-inhibitory effects of rIFN-γ EOC cells. Thus, increased arginase activity, specifically identified with arginase II, is present in most of the tested EOC cell lines. RIFN-γ inhibits or stimulates arginase activity in certain EOC cell lines, though the decrease in arginase activity does not appear to be associated with the in vitro antiproliferative activity of rIFN-γ.

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> logoff
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	44.19	44.41

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-6.80	-6.80

STN INTERNATIONAL LOGOFF AT 10:48:37 ON 27 MAY 2010